

**REDACTED DOCUMENTS RELATING  
TO DOCKET 7310**

**EXHIBIT A – Filed redacted**

**EXHIBIT B – Filed redacted**

# **EXHIBIT A**

MD ASSIST, INC

C.R. BARD, INC.

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EXPERT REPORT  
S. PARISIAN, M.D.  
March 3, 2017

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**EXPERT REPORT OF**  
**SUZANNE PARISIAN, M.D.**

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**I. PROFESSIONAL BACKGROUND & QUALIFICATIONS**

1. From 1991 to 1995, I served as a Commissioned Officer in the United States Public Health Service and achieved the rank of Lt. Commander. During that time period, I was primarily assigned to the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration (FDA). Concurrently, I was also assigned clinical responsibilities at the Armed Forces Institute of Pathology, Office of the Medical Examiner for the Armed Forces, Washington, D.C.
2. From 1991 to 1993, I was an FDA Medical Officer in the Office of Health Affairs (OHA), a staff office within the CDRH. In OHA, I provided regulatory support to both the FDA's Office of Compliance and Office of Device Evaluation (ODE). My responsibilities in OHA included health hazard and health risk assessment, Safety Alerts and physician and layperson communications, review of adverse event reports and medical literature, and review of product labeling, promotions, advertising, and corporate records as to compliance with the Food, Drug and Cosmetic Act. I was responsible for the review of mandatory adverse event reports submitted by manufacturers as well as the review of voluntary reports submitted by health care providers, patients, and others. My assignment to OHA specifically included identification and mitigation of safety issues for the public
3. From March 1993 to December 1993, I was a Medical Officer in the ODE Division of Reproductive Abdominal, Ear, Nose and Throat, and Radiology. From January 1994 through June 1995, I was one of two Chief Medical Officers in ODE.
4. I was an instructor in the FDA's Staff College to train FDA reviewers about the design and evaluation of clinical data in investigational and pre-marketing applications. I had my own primary responsibility for review of marketing applications and labeling and was required to teach medical officers the process of evaluation and review as required by the Food, Drug and Cosmetic Act for support of product marketing. I was charged with training medical officers on the process for health risk assessment and health hazard evaluation per 21 CFR Part 7.
5. Regarding post-market surveillance of marketed products, I participated with the FDA's District Offices, Office of General Counsel, and the Office of Compliance in the review of manufacturing records, labeling, product complaints, and adverse event reports obtained by the FDA. I was the primary clinician involved in several of the FDA's Major Corporate-Wide Actions for which I received various citations and honors for my services to the FDA. My awards have included Department of Health and Human Services and the Food and Drug Administration Employee of the Month.
6. After leaving the FDA, and founding MD Assist, Inc., I have continued to provide information to individuals, manufacturers, and organizations regarding the FDA's requirements; Adverse Event Reporting; and labeling, promotion, and advertising of FDA-regulated products. Those products

have included devices, biologics, and drugs approved or cleared for use and consumption for the public under various FDA processes including the 510(k) and Pre-Market Approval processes. I was also invited by the FDA to participate in a 1997 panel of experts convened by the FDA to comment on changes proposed in the requirements for medical device labeling.

7. I have continued to consult for manufacturers and lecture at conferences and seminars regarding the FDA, pre-market clearance, design of clinical trials, product labeling, Corrective and Preventive Actions, and Quality Systems. I have also been an online instructor for the Regulatory Affairs Professional Society course regarding the FDA and Medical Devices.
8. My Curriculum Vitae is attached as APPENDIX A. A list of my last 5 years of deposition and court testimony is attached as APPENDIX B. I receive \$400/hr. for study and \$600/hr. for deposition and trial testimony.

## **II. METHODOLOGY AND MATERIALS CONSIDERED**

9. I have used the same methodology I was trained to use at the FDA to reach the opinions discussed in this report regarding the design, development, and promotion of “retrievable” Inferior Vena Cava blood filters (“IVC filters” or “IVCF”) by Bard Peripheral Vascular (“BPV”) and its parent company C.R. Bard (“Bard,” collectively). I have continuously used this same methodology since 1991. This process included analyses of Bard’s communications with the FDA during the 510(k) clearance process, as well as Bard’s internal product development documents for both Bard’s retrievable IVC filters and the Simon Nitinol Filter permanent IVC filter, which Bard asserted was also the predicate for its temporary IVC filters. My review included Bard’s post-market investigation of adverse events, manufacturing and design issues with its commercial permanent and retrievable filters, and its communications of risks and benefits to its sales force, physicians, key opinion leaders, the FDA, and patients.
10. Specifically, I have reviewed Bard’s internal documents and employee testimonies listed below that were obtained through this litigation. I have also reviewed documents I obtained from the FDA’s website (<http://www.fda.gov>) or through MediRegs, Inc. (an annual subscription) or purchased from FOI Services (<http://www.foiservices.com>). Medical literature for IVC filters has been obtained from attorneys as well as through my own search of published medical and scientific literature using PubMed National Library of Medicine, National Institutes of Health (<http://www.nlm.nih.gov>). I have reviewed the following depositions of members of Bard and third-party witnesses:

- Dr. Bill Altonaga October 23, 2013;
- Murray Asch, M.D. January 5, 2011; May 15, 2016
- Bret Baird, June 9, 2016
- Christopher Aaron Beckett August 15, 2014;
- Ann Bynon, May 17, 2016
- Analise R. Cain, September 4, 2014;
- Robert Michael Carr, April 17, 2013; November 5, 2013; December 19, 2014;
- Andrzej Chandusko 10/11/2013;
- David Ciavarella, MD, 11/12/2013;

- Len DeCant, May 24, 2016
- John A DeFord, June 2, 2016
- Joseph DeJohn, June 17, 2016
- Robert DeLeon, June 16, 2016
- Mary Edwards, January 20, 2014;
- Kay Fuller, January 11, 2016;
- Clement J Grassi, M.D. July 30, 2014, August 27, 2014, and September 24, 2014
- Janet Hudnall, November 1, 2013;
- Brian Hudson, January 17, 2014;
- Abtihal Maki Raji-Kubba, July 18, 2016
- John Lehmann MD, M.P.H. April 2, 2013;
- William Little, July 27, 2016
- Judy Ludwig, July 27, 2016
- John McDermott, February 5, 2014;
- Chad Modra June 6, 2014;
- Sherri Allen O'Quinn 10/9/2013;
- Gin Schultz, January 30, 2014;
- Alex Tessmer 6/12/2013;
- Douglas Uelman, Jr. 10/4/2013;
- Carol Vierling; May 11, 2016
- Alison Walsh, 1/23/2014;
- John Wheeler, July 29, 2016

11. I have reviewed and considered the following **Nitinol Medical Technologies, Inc. (NMT)** Documents: NMT's US FDA Clinical Data Summary of the SNF(BPVE-01-00280772); SNF /Straight Line System Technical File (BPVE-01-00066044); Line Extension to the SNF/Straight Line System "Recovery Filter"(BPVE-01-00277852); NMT R&D SOP RD-SOP-050.00 RNF Design Verification November 18, 1998 (BPV-17-01-00019382);NMT RNF Animal Experiment Notes November 19, 1998, Beth Israel Hospital (BPV-17-01-00019372; BPV-17-01-00031151; BPV-17-01-00031135; BPV-17-01-00031137;BPV-17-01-00031162); April 30, 1998 NMT RNF PDT Meeting Notes (BPV-17-01-00072617);February 19, 1999 NMT PowerPoint Removable Nitinol Filter (BPVE-01-00053098) RNF Migration Study RD-SOP-035.02 June 27, 1999 (BPV-17-01-00084073); NMT R&D Technical report RNF Migration Study, Design Verification August 5, 1999 (BPV-17-01-00002650); NMT R&D Technical Report Migration Study RNF in 28mm IVC, April 7, 2000 (BPV-17-01-00067972; BPV-17-01-00072740); NMT's February 9, 2000 RNF Presentation to FDA (BPVE-01-01059494); Clinical Rationale for RNF (BPV-17-01-00045784); NMT 510(k)s; April 7, 2000 R&D Technical Report Migration Study of 30-31 Leg Span RNF in 28mmIVC. (BPV-17-01-00067972); April 14, 2000 RNF Design Review II Minutes (BPV-17-01-00034448);R&D Technical Rpt RD-RPT-137 SNF Performance Spec testing: NMT Filters (BPV-17-01-00058992). I have reviewed Dr. Morris Simon's United States Patents for the Simon Nitinol Filter (SNF) and Dr. Simon's and NMT's US Patents for 'Removable' Blood Clot Filters including the Recovery Nitinol Filter (RNF) as well as other IVC Filters Modin-Uddin Umbrella (Elgiloy) and Kimmell-Greenfield (metal coated with polymer). FDA -NMT meeting February 2000 Notes (BPV-17-01-00056843).

12. I have reviewed and relied upon the following Bard documents:

- Bard's Design, Quality Assurance and Engineering Documents:** Bard's Fact Book Project 7081 Recover Filter (BPV-17-01-00030232- 00034642); Product Performance Specification 070016 RNF and Femoral Delivery System (BPVE-01-01138018); Design Review Assessment Status December 20, 2002 (BPV-17-01-00034616); March 28, 2003 POA-7081 for RNF(BPV-17-01-00030247); November 12, 2003 Design Review for Recovery FMR Memorandum (BPVE-01-00423699); December 9, 2003 Special Design Review for RNF (Project #s 7081 and 8008) Meeting Minutes (BPVE-01-00407525; BPVE-01-00407526; 193\_Barry Exhibit.07\_1.31.14.pdf); February 23, 2004 Filter Migration Meeting Minutes from QA (BPVE-01-00438877); Test Protocol Number TPR-04-02-02 Characterization of the Recovery Filter (RF)-Migration Resistance (BPVE-01-00535555); February 25, 2004 Filter Migration Test Results (BPVE-01-00410985); March 24, 2004 Starguide Filter Migration Tests results (BPVE-01-00330122; Exhibit 10); April 1, 2004 Recovery Initiatives with RNF and Recovery Cone (BPVE-01-00268911); April 26, 2004 BPV/Angiomed Product Development Review Meeting PowerPoint (0171 Native PowerPoint); Engineering Test Reports (ETR) 04-03-02 (BPVE-01-00276094); ETR-04-03-05 GFO and NMT Manufactured Recovery Filters Migration Resistance Comparison (BPV-17-01-00153717); ETR-04-03-10 (BPVE-01-00276108); July 27, 2004 DeCant Email Regarding cava *distensibility* bench testing (BPVE-01-00009626; BPV-DEP-00014246, Tessmer Exhibit 13); Failure Investigation Report (FIR) (FIR-04-09-01) RNF-Fractures BPV-15-01-00038728; BPV-DEP-00003769; Mukherjee Exhibit 2); May 20, 2004 Wong email RE: Draft data set for statistician (BPVE-01-00511127; BPVE-01-00511131); June 9, 2004 RE: Filter Improvement DOE (BPVE-01-00009828); Bard Failure Investigations/R002 History Review (G2 Express, G2, RNF)(BPVEFILTER-01-00003802); January 19, 2005 Fasttrack G1A Filter Design Review- pre-launch design V&V review(Project #8027, RF-201F) TPR-05-01-13, ETR-05-01-06, Draft Requirements, DFMEA (BPV-17-01-00098952); G1A Filter and Femoral Delivery System -Summary of Design Changes (BPVE-01-00366486); PowerPoint Summary of G2 Design Changes (BPVE-01-00324256); January 28, 2005 G1A Recovery Filter Femoral System Design history File Meeting Minutes (Phase1) (BPV-17-01-00008926); February 10, 2005 Product Performance Spec (PPS070028)Next Generation Revision 0(BPVE-01-00004497); ETR-05-02-05 G1A RNF Femoral System Design Verification & Validation Report Project #8027-Migration Resistance @32 mm, oos filter, lower radial leg strength, ss difference Migration Resistance < SNF, only > RNF, Draft 3 failed(BPV-17-01-00001134); Product Performance Spec (PPS070028)Next Generation Revision 2 Change spec from SNF to RNF(BPVE-01-00272936); November 11, 2005 Email why Electropolishing is good(BPV-DEP-00005686; Greer Exhibit 17, Gillette Exhibit 16); February 17, 2006 RNF (Generation 1) Product Assessment Team (PAT) Minutes-Fractures(BPVEFILTER-01-00003194); February 17, 2006 RNF (Generation 1) Product Assessment Team (PAT) Minutes-Fractures(BPV-15-01-00101588; McDermott Exhibit2); March 23, 2006 Micky Graves email -G2 lack of FEA analysis for saluting arm failure would not support proposed design(BPVE-01-01225832); April 14, 2006 Draft Memo-RNF Fracture and G2 Caudal Migration update with B. Barry

(BPVE-01-00985047; Schulz-Exhibit 14); April 28, 2006 CAPA G2 (BPVE-01-00987927); September 19, 2006 G3 Caudal Project Meeting Minutes- (Indal Lapid) Project #8049 (BPV-17-01-00181885); November 27, 2006 ETR 06-08-29 Caudal Migration Test Method Development and G2 Filter Resistance Test Report Project #8049- Indal Lapid (BPVE-01-00789532); February 28, 2007 G3 Filter Concept Selection PowerPoint (369-371\_PPT\_G3); May 31, 2007 Email Shipment of 10 SNF to DNV for corrosion testing ASTM F2129-06 (BPVE-01-01351166); December 6, 2007 PowerPoint G3 Development History and Brainstorming Project #8049 (372-375\_BPVE-01-00818477); Meridian DHF Project #8120 (BPV-17-01-00149523); December 7, 2007 DNV Corrosion Testing G2 G3 Vena Cava Filters Project No.: 81174891, ASTM F2129-06, failure (BPV-17-01-00180307); June 12, 2007 email to Dr. Argarwal at CC Tech telling him to stop the SNF Corrosion testing (BPVE-01-01349522); March 2007 Recovery Filter Gen 1 Division Product Assessment SPA 04-04-01 (BPVEFILTER-01-00011272); G3 Vena Cava Filter Design Input Summary DIS-8049 (BPVE-01-0061777); September 30, 2010 Eclipse DHF, Project 8113 (BPV-17-01-00170358); Meridian Vena cava filter Product Performance Specs PPS-8120J (BPV-17-01-00148748);

- **Bard's Health Hazard Evaluation (HHEs) Documents:** March 10, 2004 RNF Migration HHE John Lehmann, M.D. (BPVE-01-00510989); April 27, 2004 Bard Recovery Filter Migration HHE (BPVEFILTER-01-00043728); June 30, 2004, RNF Migration HHE D. Ciavarella, MD to D. Uelman, QA (BPVEFILTER-01-00014836); July 9, 2004, RNF Migration HHE D. Ciavarella, MD to D. Uelman, QA (BPVE-01-000245369; BPV-DEP-00004730); November 17, 2004 from David Ciavarella, MD to Doug Uelman, QA, HHE- updated re: Limb Fractures of RNF (BPVE-01-00103875); December 17, 2004 from David Ciavarella, MD to Doug Uelman, QA, 76 reported serious hazards HHE (BPVE-01-01019821); February 15, 2006 G2 IVCF-Migration (BPVEFILTER-01-0008355); June 10, 2004 email Recovery Filter/Detachments (BPV-DEP-00004807; BPVE-01-00509497, Exhibit 8);
- **Bard's Remedial Action Plans (RAP) and Crisis/Communication Plan Documents:** February 10, 2004 Sales Force (BPV-17-01-00164702); February 27, 2004 Case for Caval Centering (BPVE-01-00373887); April 21, 2004 Bard Recovery Filter Migration Remedial Action Plan (RAP) (BPV-17-01-00153578; BPVE-01-00433210); March 19, 2004 Recovery Crisis Communication Plan email (BPVEFILTER-01-00043824); Notes from RNF/Clinical Panel Review (BPV-17-01-00097817); June 24, 2004 D. Ciavarella email RE: RNF discussion with Dr. Mishra (BPVE-01-00163350); July 15, 2004 Hudnall – Complications Q&A (BPVE-01-00268921 DeJohn Exhibit 348, see also BPVE-01-00492578); August 30, 2004 Internal Q&A Sales (BPVE-01-00033810); September 23, 2004 draft Dear Doctor Letter (BPVE-01-00037324; Exhibit 24); Hudnall's Information for Use Update (BPVE-01-00303515); December 1, 2004 Revised RAP (BPVE-01-00435296); January 4, 2005 RNF Migration RAP SPA-04-12-01 (BPVE-01-01019773); August 25, 2004 Hudnall email RE: Recovery Filter Objective Statement (Snare-based retrieval system) (BPVE-01-00008821); January 4, 2005 Recovery Filter migration RAP SPA-04-12-01 (BPVE-01-01019773); February 11, 2005 RE: VENA CAVA

FILTER- stock recovery for G1A (BPVE-01-00167251); February 14, 2005 Recovery Transition Plan (BPVE-01-00171311); July 16, 2005 Westy's Situation -MAUDE (BPV-DEP-00005665; Goodrow Exhibit 30); August 18, 2005 Doctor letter communication Pt loss (BPV-DEP-00004802; BPVE-01-00244630, Friedman Exhibit 6); November 10, 2005 Email about G2 v Maude (BPV-17-01-00096991); November 30, 2005 G2 v MAUDE email (BPVE-01-01511164); December 6, 2006 Addendum BPV RAP Limb Fractures SPA 04-04-01(BPVE-01-00299538; BPV-DEP-00004836); December 19, 2005 RF Limb detach email (BPVEFILTER-01-00002447, Schulz Exhibit 13); January 31, 2006 Caudal email(BPVE-01-01025389); March 23, 2006 Historical FEA Analysis G2(BPVE-01-01225832); July 18, 2006 Quality Management Board Review(BPVE-01-00987997); July 2, 2010 Meridian Claims (BPVE-01-02030532);

- Bard Executive Summaries and Presentations for Management:** April 23, 2004 MAUDE 2004 (BPVE-01-00268632, Ciavarella Exhibit 23); April 26, 2004 BPV/Angiomed New Product Review meeting PowerPoint(April 26, 2006 BPV-ANGIOMED); July 12, 2004 of RNF AEs (migration and fracture)-Executive Summary (BPVE-16-01-00102078; BPV-DEP-00021413); August 26, 2004 Corporate Presentations (BPVE-01-00009466, Tessmer Exhibit 19); Bard November 1, 2005 Spreadsheet "RNF Detached Limbs" (BPV-17-01-00035618); RNF (RF048F)-R002 2004-2005 Chronology of Events-G2 Release(BPVEFILTER-01-00002824); April 19, 2005 IVC RNF Adverse Events (Migrations/Fractures)- Executive Summary MAUDE Comparative (BPVE-01-00434275); May 19, 2005 G2 Caudal Summary ppt, RNF Fx Rpt (BPVE-01-01511339; Schulz Exhibit 15; J. Sullivan Exhibit 445) June 6, 2005 Hudnall- Forecast email (BPVE-01-00338862); August 3, 2005 IVC RNF AEs(Migration/Fractures)-Executive Summary; BPVE-01-00665789 PowerPoint Strategy; December 27, 2005 G2 Caudal Migration email (BPV-DEP-00004804; BPVE-01-00245186); March 29, 2006 Quality Management Board Review (BPVE-01-00988894); June 1, 2006 G2Caudal Migration Failure Investigation Meeting Summary(BPV-17-01-00155086); October 22, 2007 Everest -revised Migration section(BPVE-01-01455684); November 30, 2008 Draft G2 and G2X Fracture Analysis(BPVE-01-00714617); November 16, 2009 Nicholson talking points (BPVEFILTER-01-00203546); Idea POA Eclipse Anchor Filter (BPVE-01-02077858); August 7, 2010 RE: York Chronology(BPVE-01-01526379); Everest Complications PowerPoint(BPV-17-01-00188507); Funding for the Denali-Next Gen Filter (BPVE-01-00666685); 2010 Franchise Reviews Filters Shoot the Gaps (BPVE-01-00559941); October 2000 Regulatory Affairs Manual Product Remedial Actions -Recall (BPV-17-01-00024667); September 2, 2005 G2 Filter FAQs (BPV-17-01-00062020);
- Bard and FDA Interaction documents:** March 15, 2002 Dr. Asch protocol (BPV-17-01-00052583); Tilted Retrieval Pt 33 Report April 18, 2002 (BPV-17-01-00055205); June 2002 emails RE: CDRH's Request for SNF from Bard (BPV-FULLER-00002251 Recovery Filter 510(k)s (BPV-17-01-00057958; BPV-17-01-00057953; BPV-17-01-00057926; BPV-TRIAL EXHIBIT-1245); August 5, 2002 FDA Req AI K022236(BPV-FULLER-00002320); August 12, 2002 FDA TC (BPV-01-00059159); August 30, 2002 Response to August Req (BPV-FULLER-

00002303); September 19, 2002 Memo Regulatory Status (BPV-17-01-00031032); November 27, 2002 Special K022236 (BPV-FULLER-00001375); October 4, 2002 FDA req Addit Inform (BPV-17-01-00057733); October 6, 2004 Mary Edwards' Bard Letter to FDA regarding IFU for RNF retrieval option RE: K031328 (BPV-17-01-00061618); October 25, 2002 Response to FDA (BPV-FULLER-00002276); December 17, 2002 Request for FDA RNF meeting (BPV-17-01-00062069); January 14, 2003 FDA Bard RNF meeting with Alpert (BPVEFILTER-01-00147182); Previous Correspondence RNF Abbreviated 510(k) (BPV-17-01-00054429); July 1, 2003 clarification (BPV-17-01-00054093); July 2, 2003 email clarification K031328 (BPV-17-01-00058144); July 24, 2003 Re changes to RNF label (BPV-17-01-00054098); July 25, 2003 K031328 Clearance (BPV-17-01-00058122); January 21, 2005 FDA Contact Report with Allen and FDA's L Kennel (ODE)'RNF Update' - commitment to clinical registry (BPV-17-01-00102065); Notes FDA Meeting March 24, 2005 (BPV-17-01-00045882); February 8, 2005 FDA Contact Report RNF-Update Bard's Allen and FDA's J.Liu (BPV-17-01-000000210); March 18, 2005 Traditional 510(k) RF-201F (BPVE-01-00005831); May 2, 2005 Brian Barry email-No Competitive Filter data provided to FDA at meeting (Barry Exhibit 5); April 25, 2005 Bariatric email- rationale for no boxed warning (Hudnall Exhibit 12); March 2, 2005 Special K050558 G2 Filter (FDA\_PRODUCTION\_00000050; BPV-FULLER\_000005720; FDA\_PRODUCTION\_00000048; BPV-FULLER\_000005718); March 30, 2005 request for AI, May 6, 2005 Teleconference with FDA, June 3, 2005 Response to FDA AI Special 510(k) K050558- request conversion to a Traditional 510(k)-change RF210 to 'RF 310' (BPV-17-01-00046553); June 6, 2005 email Bard June 3, 2005 Draft Clinical Protocol for EVEREST IDE ( K050558) (BPV-17-01-00056051) July 8, 2005 IDE Application (Everest) (BPVE-01-00030385); July 8, 2005 IDE G050134 (BPV-17-01-00131662); Special K052578 G2 Filter Jugular/Subclavian Delivery Kit (Project #8002) (BPV-17-01-00046759); October 3, 2005 Bard Response to FDA's 8/5/05 for IDE G050134 (BPV-17-01-00045007); FDA email and TC with Bard October 14, 2005 G2 Biocompatibility testing (BPVE-01-00376010); July 30, 2008 Special 510(k) K080668 G2 Express; October 31, 2008 K082305 G2 Express; April 30, 2009 Everest Final Study report (BPVE-502d-0000011); January 7, 2010 FDA Contact Report Recovery/G2/G2X Fractures and Nicholson publication/presentation (BPVEFILTER-01-00320910); January 14, 2010 Special 510(k) K093659 Eclipse; IDE Supplement Response G2 Filter Clot Trapping Efficacy Protocol to G050134 Testing Results (BPV-17-01-00123538); June 25, 2010 K101431 ECLIPSE Filter System; August 24, 2011 K102511 Meridian Filter System; May 15, 2013 K130366 Denali Filter System;

- **Brochure:** Recovery G2, G2X (BPV-17-01-00137588); G2 Filter System (BPV-17-01-00142912); Recovery IFU (BPV-17-01-00042515); Recovery revised IFU (BPV-17-01-00042650); Recovery IFU (BPVE-01-00435559); G2 Filter System (BPV-17-01-00137624); G@ Patient Q&A (BPV-17-01-00137624);
- **Medical Literature addressing Bard IVC filters:** Becker D. et.al. Inferior Vena Cava Filters Indications, Safety, Effectiveness. *Arch Intern Med* October 1992, Vol 152: 1985-1994. Simon M. Rabkin DJ, Kleshinski S, Kim D, Ransil BJ Comparative

evaluation of clinically available inferior vena cava filters with an in vitro physiologic simulation of the vena cava. *Radiology*. 1993 Dec;189(3):769-74; Grassi CJ, Swan TL, et al For the Society of Interventional Radiology Standards and Practice Committee. Quality Improvement Guidelines for Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism. *J Vasc Interv Radiol* 2001; 12:137-141; Grassi CJ, Swan TL, et al For the Society of Interventional Radiology Standards and Practice Committee. Quality Improvement Guidelines for Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism. *J Vasc Interv Radiol* 2003; 14: S271-S275; Asch MR. Initial experience in humans with a new retrievable inferior vena cava filter. *Radiology* Dec. 2002; 225(3):835-44 (DOI:10.1148/radiol.2252011825); Cheung MC, Asch MR, Gandhi S, Kingdom JCP. Temporary inferior vena caval filter use in pregnancy. *J Thromb Haemost* 2005; 3:1096-7; Kalva SP, Athanasoulis CA, et al. "Recovery" vena cava filter: Experience in 96 patients. *Cardiovasc Interv Radio* 2006 Jul-Aug; 29(4):559-64. Berczi V, Bottomley JR, et al. Long-term retrievability of IVC filters: should we abandon permanent devices? *Cardiovasc Interv Radiol* 2007 Sep-Oct;30(5):820-7. Hull JE, Han J, Giessel GM Retrieval of the Recovery filter after arm perforation, fracture and migration into the right ventricle. *J Vasc Interv Radiol* 2008 Jul;19(7):1107-11. Seshadi T, Tran H, Lau KK et al. Ins and Outs of inferior vena cava filters in patients with venous thromboembolism: the experience at Monash Medical Center and review of the published reports. *Intern Med J* 2008 Jan; 38(1):38-43. Hull JE, Robertson SW Bard Recovery filter: Evaluation and management of vena cava limb perforation, fracture, and migration. *J Vasc Interv Radiol* 2009 Jan; 20(1):52-60. Binkert CA, et al. Technical Success and Safety of Retrieval of the G2 in Prospective, Multicenter Study, *JVIR* 2009;20:1449-1453. Nicholson W et. al. Prevalence of Fracture and Fragment Embolization of Bard Retrievable Vena Cava Filters and Clinical Implications Including Cardiac Perforation and Tamponade. *Arch Intern Med* November 8, 2010; 170(20):1827-1831 (online August 9, 2010). Morales JP et al. Decision analysis of retrievable inferior vena cava filters in patients without pulmonary embolism. *Jour Vasc Surg: Venous & Lymph Dis* 2013; Vol 1(No.4):376-84(UCM396384) FDA's published review recommending removal 29 to 54 days after the transient risk of PE has passed. Grewal S, Charnathy MR. Kalva SP. Complications of Inferior Vena Cava Filters, *Cardiov Diag & Ther*. 2016;6(6):632-641. Stavropoulos SW, Chen JX, et al. DENALI Trial Investigators Analysis of the Final DENALI Trial Data: A Prospective, Multicenter Study of the Denali Inferior vena cava Filter. *J Vasc Interv Radiol* 2016 Oct; 27(10):1531-1536. Reis SP, Kovoor J, Kalva SP Safety and Efficacy of the Denali Inferior Vena Cava Filter: Intermediate Follow-Up Results. *Vasc Endovasc Surg* 2016 Aug; 50(6):385-90.

13. Regarding the FDA's documents I have reviewed: FDA's November 26, 1999 Guidance for Industry and FDA Reviewers/Staff "Guidance for Cardiovascular Intravascular Filter 510(k) Submissions; May 6, 2014 "FDA Safety Communication: Removing Retrievable Inferior Vena Cava Filters updating FDA's August 9, 2010 Initial Communication"; Decision Analysis of Retrievable Inferior Vena Cava Filters in Patients without Pulmonary Embolism; FDA's 522 Order for Postmarket Surveillance Studies for Bard's IVC Filter; PRESERVE Study Proposal, and Morales (2013); May 6, 2014 FDA Updated Safety Communication "Removing Retrievable

IVC Filters”; FDA’s July 13, 2015 WARNING LETTER to Timothy Ring, Chairman and CEO C.R. Bard; FDA’s December 16, 2016 CLOSE OUT LETTER to Timothy Ring, Chairman and CEO C.R. Bard; .

14. I have also reviewed and relied upon the following Expert Reports and Expert depositions:

- February 27, 2014 Expert Report of Christine L. Brauer, Ph.D. and deposition
- April 9, 2014 and February 24, 2015 Expert Reports of Donna-Bea Tillman and deposition June 12, 2014;
- August 28, 2016; January 27, 2017 Rebecca Betensky, Ph.D. Expert Report; Deposition Rebecca Betensky, Ph.D. July 26, 2016
- Mark Eisenberg, M.D., M.P.H., August 17, 2016
- September 2016 Expert Report of David Kessler, M.D.

### **III. SUMMARY OF OPINIONS**

#### **A. OPINION #1: Bard’s premarket actions with design and development of the RNF as a permanent IVC filter were inadequate.**

Based on Bard’s documents and employee testimonies, Bard knew its Recovery Nitinol IVC filter (RNF) was not “*substantially equivalent*” to the Simon Nitinol IVC Filter (SNF), which was purportedly the appropriate predicate device for Bard’s family of RNF permanent and temporary IVC Filters. Bard possessed data showing that the two products did not behave the same in patients when used as permanent filters before Bard obtained FDA clearance to market the RNF as a permanent IVC filter based on the SNF as the predicate device. Yet Bard’s employees certified to the FDA that the RNF was substantially equivalent to the SNF and that the RNF raised no new issues of safety and effectiveness when implanted as a permanent IVC filter in a patient in order to obtain FDA clearance to start commercially marketing the RNF in the United States. Shortly after Bard introduced the RNF commercially as a permanent and then later as a temporary filter, Bard began to receive reports of serious patient injuries and deaths associated with the RNF, which had not been seen with the SNF. It was only after receipt of patient deaths and serious injuries from its own Key Opinion Leaders (KOLs) that Bard begin to question the adequacy of the RNF’s original design, its propriety for clinical use, and the validity of its pre-clinical performance testing. These premarket errors and omissions did not comply with FDA regulations, Bard’s own internal operating procedures, or acceptable industry practices for marketing safe and effective permanently implanted medical devices.

***Applicable Regulations:*** 21 CFR § 807; 21 CFR § 860; 21 CFR § 820; 21 CFR § 806; 21 CFR § 801.109; 21 USC § 331(a)(b); 21 USC § 352(a)(f)(1)(2),(t); 21 USC § 321(n); 21 USC § 351

**B. OPINION #2: Bard obtained FDA clearance to market the RNF as both a permanent and retrievable IVC filter yet failed to provide physicians and patients with adequate, updated “Instructions For Use” and “Warnings of Risks.”**

Bard, not the FDA, is responsible for ensuring the adequacy of its labeling and marketing. To obtain clearance for the RNF from the FDA, Bard claimed it was substantially equivalent to the permanent SNF, despite not having data to support safe and effective permanent use. Bard’s labeling and marketing failed to adequately instruct (IFU) and warn implanting physicians, physicians caring for permanently implanted patients (e.g., surgeons, hematologists, internists, emergency medicine), and patients about the potential post-market risks, including the need for the patient to continue to be monitored for filter complications and the need for appropriate placement (stability) when permanently implanted. When Bard had the RNF cleared for the “option” to be used as a temporary IVC device, Bard continued to fail to adequately and voluntarily update its labeling, IFU, and warnings to include recommendations for indwell time range and warnings describing updated post-market risks. Bard, not the FDA, was required to provide implanting physicians, retrieving physicians, and physicians caring for implanted patients with an updated labeling describing risks of tilt, migration, fracture, embolization; difficulties with retrieval perforation; the potential for revision surgery; and the need to plan for removal of the RNF filter when no longer clinically indicated.

*Applicable Regulations:* 21 CFR § 807; 21 CFR § 801.109; 21 USC § 331(a)(b); 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n)

**C. OPINION #3: Bard’s actions for post-market oversight continued to permit marketing of the flawed RNF as a permanent IVC filter.**

Despite obtaining RNF 510(k) clearance from FDA by asserting that the RNF was substantially equivalent to the SNF permanent IVC filter, Bard quickly learned that when the RNF was implanted in living patients it failed at much higher rates and produced significant complications much greater than occurred with the SNF. Despite the foreseeable risks for patients, Bard continued to sell the RNF without providing adequate warnings to physicians regarding the RNF’s risks, the need to continue to monitor patients after implanted with the RNF, difficulties with retrieval, and the need to remove the RNF from a patient as soon as clinically feasible. Bard’s marketing activities and plans downplayed the risks for implanted filters with device aging and overstated benefits to its sales force and physicians. Furthermore, Bard Marketing’s off-label promotion expanded the population of patients implanted with the RNF into new and healthier patient populations beyond its cleared indications for use, while at the same time failing to protect and warn physicians and patients about the true risks of complications, reported failures, revision surgery and death with the RNF.

**Applicable Regulations:** 21 USC § 331(a)(b); 21 CFR § 803; 21 CFR § 801.109; 21 USC § 352(a)(f)(1)(2)(t); 21 USC § 321(n); 21 USC § 351; 21 CFR part 7; 21 CFR part 820; 21 CFR § 806

**D. OPINION #4: Bard developed its “Next Generation” of filters based on piecemeal reactive modifications to its flawed original RNF filter platform rather than using quality science and medical device design principles.**

Bard provided inaccurate and misleading information to the FDA, physicians, and the public regarding the safety and efficacy of its RNF permanent and retrievable filters. Despite its marketing claims, the later iterations of its IVC filters continued to rely on the original flawed RNF platform, but now used as a predicate device. Bard’s IVCF practices overstated benefits and downplayed risk with the introduction of each new member of its commercial family of filters. IVCF changes were made in a piecemeal and reactive fashion heaped onto a flawed underlying RNF platform with a goal to address physician perceptions about improvement to the prior generation of product. Use of new tradenames inaccurately implied improved quality from the prior generation. Based on the internal documents and employee testimonies reviewed, Bard’s evolution of changes starting with the RNF were not primarily made to improve quality, safety, and efficacy or to protect patients but rather primarily to address sales force and physician perceptions about device problems and help keep and expand market share.

**Applicable Regulations:** 21 CFR § 820.198; 21 CFR § 820.30; 21 CFR § 820.100; 21 CFR § 820.75; 21 CFR § 820.250; 21 USC § 352(a)(f)(1)(2)

**E. OPINION #5: Bard’s Quality Systems (QS) and post-market monitoring procedures were flawed, helped underestimate patient risk, and permitted continued commercial release of misbranded and dangerous products as supported by Bard’s receipt of an FDA 2015 Warning Letter.**

FDA issued a July 13, 2015, Warning Letter to Bard following inspections in 2014 of its Glens Falls, New York and Tempe, Arizona facilities. FDA observed serious problems in Bard’s manufacturing and quality management systems. Problems identified included Adulteration/Misbranding violations, Quality Systems Regulation violations, and Medical Device Reporting violations. The observations identified by the FDA’s inspector are consistent with Bard’s employee testimonies and Bard’s internal regulatory documents.

**Applicable Regulations:** 21 CFR § 820.198; 21 USC § 352(t)(2); 21 USC § 360i, 21 CFR Part 803; 21 CFR § 820.50(a) 21 CFR § 820.75(a); 21 CFR § 820.80(b); 21 CFR§§ 803.50(a)(2), (b)(2)(3); 21 USC § 331(a)(b)

**F. OPINION #6: Bard engaged in aggressive off-label promotion which overstated benefits, downplayed risks, expanded the implanted patient population and failed to adequately warn physicians, patients, and its own sales force of the risks.**

Bard engaged in improper and illegal promotion and marketing of its RNF filters for off-label uses which changed the intended patient population and expanded the number of new and healthier patients unnecessarily implanted with defective Bard IVC Filters. Such actions began prior to Bard's 510(k) clearance of the RNF and continued throughout Bard's aggressive promotion of the RNF family of IVC Filters all without providing adequate risk information to physicians or patients.

**Applicable Regulations:** 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n); 21 CFR § 801.109; 21 USC § 351(f)(1)(B); 21 USC § 360(e); 21 USC § 360(k); 21 CFR § 807.81(a)(3)(ii); 21 CFR § 801.4

**G. OPINION #7: Bard marketed the Recovery Cone Retrieval System as part of the RNF IVCF system to facilitate filter retrieval without having first obtained 510(k) clearance to do so.**

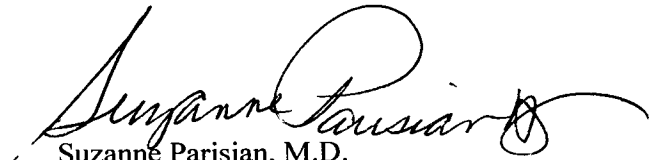
Bard marketed a Recovery Cone Removal System in the United States as part of the RNF IVC filter system for retrieval without first obtaining the required pre-market clearance. It continued to market defective Recovery Cone Removal Systems without conducting a voluntary recall or notifying physicians of the risks.

**Applicable Regulations:** 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n); 21 CFR § 801.109; 21 USC § 351(f)(1)(B); 21 USC § 360(e); 21 USC § 360(k); 21 CFR § 807.81(a)(3)(ii); 21 CFR § 801.4

**IV. SIGNATURE**

15. My opinions are all made to a reasonable degree of medical and regulatory certainty.

16. I reserve the right to amend my opinion and supplement my report at a later date.

  
Suzanne Parisian, M.D.  
March 3, 2017

**V. Brief Overview of the FDA's and Medical Device Manufacturer's Roles Pursuant to the Federal Food, Drug and Cosmetic Act (FDCA)**

**A. The pre-market 510(k) clearance process<sup>1</sup> is based on the concept of substantial equivalence.<sup>2</sup>**

17. The FDA is the United States Congress' implementer of FDCA. Since 1976, the FDA has been assigned to be a medical device gatekeeper for the public and to oversee the commercial availability and entry of new commercial medical devices into the public market. In that role, the FDA is responsible for the premarket review and clearance of new devices. Once a new device is cleared, it essentially will stay on the market until withdrawn by the manufacturer; there is no further FDA regulatory action required to review 510(k) cleared products.
18. The FDA's pre-market role for non-exempted devices includes a process to review a sponsor's premarketing submissions to determine the intended use(s) of the proposed new device and to see if there are other devices marketed for the same intended use, a/k/a predicate devices. The FDA must also determine whether the new device raises new issues of safety and effectiveness that still need to be addressed by the sponsor.<sup>3</sup> The FDA determines the claims which can be made by a sponsor in its label and when marketing the new device. If all of these issues appear to have been successfully addressed by the sponsor, the FDA clears the 510(k) for marketing of a new device that is intended to perform in patients as described in the sponsor's submission. Devices that are "substantially equivalent" to previously-cleared or approved predicate devices in terms of risk are regulated with the same type of manufacturing controls. With the current 510(k) process, the manufacturer returns to FDA's premarket reviewers in CDRH's Office of Device Evaluation (ODE) only when it wishes to make significant modifications to an already cleared device, change marketing claims, address a safety or performance issue, or request clearance of a new generation of devices or technology. The FDA's ODE reviewer role is "premarket clearance," the FDA has no post-market oversight role for 510(k)s or medical devices.
19. Both 510(k) clearance submissions and Pre-Market Approval application submissions must have a signed Truthfulness and Accuracy Statement for the submission to be filed with FDA for review

**1. 510(k) clearance is *not* the same as approval by the FDA.**

20. Upon obtaining FDA's 510(k) clearance, the manufacturer becomes responsible for the sale of its product and ensuring the safety of the device throughout its commercial and intended lifespan.

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<sup>1</sup> The term "510(k)" refers to Section 510(k) of the FDCA (21 USC 360(k)), Registration of Producers of Drugs and Devices. The statute describes that "each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use, shall, at least 90 days before making such introduction or delivery, report to the Secretary- (1) the class in which the device is classified...(2) action taken by such person to comply with the requirements under section 514 or 515 that are applicable to the device."

<sup>2</sup> 21 USC § 360c(i).

<sup>3</sup> 21 CFR§ 860.7.

After clearance, the public will begin to have wider exposure to the new device. Unlike the Pre-Market Approval process,<sup>4</sup> which is much more involved and if completed results in the FDA's actual approval of the medical device as safe and effective and also establishes the controls necessary for manufacturing, there is no required post-market reporting back to ODE. The '510(k) Clearance Letter' is merely the FDA's license for a sponsor to begin marketing the cleared device for the intended use and claims as stated to the FDA in the 510(k) submission.

21. The FDA's 510(k) clearance letter indicates that it is "misbranding" for a sponsor to indicate that FDA has "approved" its cleared device (underlining for emphasis):

*Submission of a premarket notification in accordance with this subpart, and a subsequent determination by the Commissioner that the device is intended for introduction into commercial distribution is substantially equivalent to a device in commercial distribution before May 28, 1976, or is substantially equivalent to a device introduced into commercial distribution after May 28, 1976, that has subsequently been reclassified into class I or class II, **does not in any way denote official approval of the device. Any representation that creates an impression of official approval of a device because of complying with the premarket notification regulations is misleading and constitutes misbranding.***<sup>5</sup>

22. The 510(k) process is a paper submission from the sponsor. The FDA does not review, inspect or test the proposed new device. The FDA does not conduct any independent testing of the device. There is no FDA hospital or FDA clinic for device testing. FDA must rely on the truthfulness and accuracy of the 510(k) sponsor to provide the FDA's reviewers with the relevant information to determine if there are new issues of safety and effectiveness which first need to be addressed by the sponsor for a product for an intended use that raise new question of safety and effectiveness compared to the cited predicate. FDA requires the sponsor of the 510(k) to sign a Truthful and Accurate Statement certifying that no material facts have not been provided to FDA in the submission.

**2. Devices that have been cleared by the FDA but which do not perform as represented to FDA are "adulterated" products.**

23. Under section 510(k), a person intending to introduce a device into commercial distribution is required to submit a premarket notification to the FDA at least 90 days before the start of commercial distribution. Section 513(i)<sup>6</sup> of the Act states that the FDA may issue an order of substantial equivalence only upon making a determination that the device to be introduced into commercial distribution is as safe and effective as a legally marketed device. Under 21 CFR § 807.87, the FDA establishes the content requirements for premarket notifications to be submitted by device manufacturers in a 510(k) for a sponsor to help support of a substantial equivalence decision from the FDA. However, the FDA has been given discretion in the type of information

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<sup>4</sup> 21 CFR § 814; 21 USC § 360e.

<sup>5</sup> 21 CFR § 807.97.

<sup>6</sup> 21 USC § 360c(i) ("Substantial equivalence").

that it deems necessary to meet those content requirements for support of substantial equivalence. This allows the FDA flexibility to change its requirements or request additional information.

24. If a new device does not perform as represented to (and cleared by) the FDA in a 510(k) submission, it is considered “adulterated.”<sup>7</sup> It is not the same device cleared in the 510(k).

### 3. FDA Classifies Medical Devices Based on Risk and Manufacturing Controls<sup>8</sup>

25. The FDA’s process for handling medical devices post 1976 is considered “risk-based.” The agency, based on potential risk for patients and the types of manufacturing controls necessary to control these risk, assigns types of products into certain classes, with Class III (highest risk), Class II Moderate risk (most devices cleared by 510(k)) and Class I (lowest risk). All devices of the same type and class will have the same types of requirements for manufacturing controls. FDA is permitted to exempt certain Class II (and most Class I) devices from the need to obtain FDA pre-market 510(k) clearance prior to marketing. There are reservations for certain exempted devices if there are new issues of safety and effectiveness.

26. The FDA’s 510(k) application review process is to entail (underlining added for emphasis):

...  
(b) FDA will determine that a device is **substantially equivalent** to a predicate device using the following criteria:

(1) The device has the same intended use as the predicate device; and

(2) The device:

(i) Has the same technological characteristics as the predicate device; or

(ii)

(A) Has different technological characteristics such as significant change in materials, design, energy source, or other features of the device from those of the predicate device;

(B) The data submitted establishes that the device is substantially equivalent to the predicate device and contains information, including clinical data if deemed necessary by the Commissioner, that demonstrates that the device is as safe and as effective as a legally marketed device; and

(C) Does not raise different questions of safety and effectiveness than the predicate.

(3) The predicate device has not been removed from the market at the initiative of the Commissioner of the Food and Drugs or has not been determined to be misbranded or adulterated by a judicial order.<sup>9</sup>

<sup>7</sup> 21 USC § 351(f)(1).

<sup>8</sup> 21 CFR 860.3 Definitions

<sup>9</sup> 21 CFR § 807.100

**4. Prescription medical devices require an adequate prescription label.**

27. FDA does not usually engage in issues involving the practice of medicine. A device is classified as a prescription device if the intended user of the device must have additional training, i.e., the device is not intended to be used by a layperson without the involvement of a health care provider. It is each State and not the FDA that determines the training necessary for an individual to be able to write prescriptions and use a prescription device. Not all prescription devices are intended to be used only by physicians.
28. Devices that do not provide adequate instructions for use (“IFU”) and warnings for the intended user are considered misbranded.<sup>10</sup>
29. Marketing that makes new claims or changes the intended use of the device beyond what is provided in the IFU are also misbranded. If the device is not either cleared or approved for that new indication, the sponsor is marketing an adulterated device.<sup>11</sup>
30. To make a determination of misbranding, the FDA will review all information written, oral or implied about a product from the sponsor as well as its agents, including physicians.<sup>12</sup>
31. Prescription device labeling must comply with implementing regulations for prescription labeling, including marketing materials, publications and CME generated, and statements of the sponsor’s physician trainers and sales force, including at public meetings.<sup>13</sup>
32. It is a Prohibited Act (under the Food, Drug and Cosmetic Act) for any manufacturer to sell a medical device in the United States that is not safe and effective and adequately labeled.<sup>14</sup> FDA and the Act place the duty for ensuring the accuracy and adequacy of the product’s label and labeling as well as safety and efficacy on the manufacturer. The manufacturer, not the FDA, is responsible for its device and its labeling.

**5. In administering the 510(k) process, FDA’s device reviewers are required to use the “least burdensome” method for industry.**

33. The FDA was given a legal mandate from Congress in 1997 to make the 510(k) process the “Least Burdensome” for the sponsor.<sup>15</sup> Following the passage of the Medical Device User Fee Amendment (MDUFA), the FDA’s reviewers are committed—in return for medical device industry user fees to provide funds for device reviewers—to improvement in the efficiency of its

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<sup>10</sup> 21 USC § 352(f)(1),(2); 21 USC §321(n)

<sup>11</sup> 21 CFR § 801.4; 21 USC§ 351

<sup>12</sup> 21 USC § 321(n)

<sup>13</sup> 21 CFR § 801.109.

<sup>14</sup> 21 USC § 33(a)

<sup>15</sup> Least Burdensome Provisions of the FDA Modernization Act of 1997

review and clearance activities. CDRH's improved efficacy is to result in an increase in completion of the 510(k) review process within the mandatory 90 days.<sup>16</sup>

34. The post-marketing reporting of the sponsor to the FDA on 510(k)-cleared devices is intended to be similarly "least burdensome." Post-market reports of adverse events (Medical Device Reports or MDRs), 21 CFR § 803, are submitted by the sponsor to the FDA as mandatory reports and voluntarily reports by healthcare providers, hospital risk managers, patients to the FDA's database should also be tracked and submitted. The MDRs are not intended to go to pre-market reviewers in ODE, but are reviewed by post-market reviewers in the Office of Compliance (OC). OC staff is tasked with post-market monitoring of commercial medical devices. The manufacturer, not the FDA, is required to have methods in place for complaint handling, post-market surveillance, statistical trending, corrective and preventive actions, medical device reporting, and updating its sales force and labeling as part of required Quality Systems (QS). The manufacturer (who is selling the device and involved with the device day-to-day) is assigned the bulk of the post-market duty to voluntarily ensure its commercial product remains safe and effective by monitoring performance, and ensuring adequate labeling.
35. The 510(k) holder is typically able to update its own labels, warnings, instructions for use, patient brochures, training manuals, labeling and marketing with no involvement from the FDA.

#### **6. New Medical Devices Obtain FDA's 'Approval' Through Premarket Approval Applications (PMA).**

36. In contrast to the 510(k) route to market, the Pre-Market Approval Application (PMA)<sup>17</sup> process uses a series of clinical trials<sup>18</sup> to help support safe and effective performance of the initial device in patients and for obtaining FDA's approval. A PMA approval establishes the manufacturing controls necessary for producing and selling commercial devices that are reasonably safe and effective. The PMA process requires additional conditions for PMA approval, including requirements for periodic reporting to FDA, and approval and updating of labels and marketing and post-market surveillance. Subsequent changes and modification to a PMA approved product are made by a sponsor's obtaining FDA's approval of a PMA supplement.<sup>19</sup>

#### **B. Post-market, the medical device manufacturers are required to develop internal design and process controls and methods for post-market surveillance, recalls, and notifications to adhere to FDA's quality systems regulations (GMP/QS).<sup>20</sup>**

37. It is a manufacturer's post-market role to ensure that any 510(k) cleared device sold in the United States remains safe and effective, adequately labeled, adequately manufactured, and monitored. Each manufacturer has a post-market role for continued surveillance to actively monitor the

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<sup>16</sup> Medical Device User Fee and Modernization Act (MDUFMA) of 2002 (Public Law 107-250), renewed Medical Device User Fee Amendments of 2007 (MDUFA)

<sup>17</sup> 21 CFR § 814

<sup>18</sup> 21 CFR § 812

<sup>19</sup> 21 CFR § 814.39

<sup>20</sup> 21 CFR part 820; 21 CFR § 803; 21 CFR § 806; 21 Part 7

acceptable performance of its device throughout the entire anticipated lifetime. The manufacturer—not the FDA—is to ensure continued patient safety and that the device performs consistent with FDA’s 510(k) clearance.

38. Therefore, the primary role for oversight of a device sold in the United States belong to the company. By selling a permanently implanted commercial device like an IVC filter, Bard assumed responsibility for monitoring and oversight of its product, which extends over the anticipated life expectancy of the device, in this case the patient’s life. This is referred to as a responsibility which extends over the Total Product Life Cycle (TPLC). TPLC requires Bard to be involved with its IVC Filters long after obtaining FDA’s 510(k) clearance. There is no periodic FDA review required of 510(k)-cleared products, nor is there a mechanism for FDA to remove 510(k) clearances. Once a product is 510(k)-cleared the FDA’s pre-market review role is completed.
39. Bard, not the FDA, is responsible for ensuring the continued adequacy of its IVC filter design, materials, and processes for manufacturing and product release. Bard is also responsible for developing its own procedures and standards to adhere to adequate manufacturing controls, using statistical methods to identify issues with its device, opening Corrective and Preventive Actions, conducting failure investigations to address safety issues, reporting any issues to the FDA, and communicating with physicians and its own sales force about issues with its device. Bard is required to update its product labels and marketing to ensure public safety and compliance with the Act.
40. The FDA becomes involved with protection of the public when it becomes aware of unaddressed safety issues for a device and/or similar device technology. An example is what occurred on August 9, 2010, when the FDA issued “FDA’s Safety Communication for long-term risks of IVC filters.”
41. Bard as the manufacturer is responsible for developing its own effective and adequate standard operating procedures (SOP) to meet at least minimum Good Manufacturing Practices of the Quality Systems Regulations (GMP/QS) for the production and monitoring of its commercial products.<sup>21</sup> The QS for production of devices required each manufacturer to have established its own written standard operating procedures (SOP) and processes and adhere to them as it manages design and development of products sufficient to ensure its continued compliance with the Act. The duty to ensure the adequacy of the design and development procedures and monitoring practices established, as well as the duty to ensure the adequacy of personnel training and support for these quality processes, rests with a manufacturer’s executive management (top- down responsibility).
42. The process used for making “device modifications” to already cleared devices is to include as part of QS standard effective procedures used for documentation of design inputs, risk analysis, design output, test procedures, verification and validation procedures and documentation of formal design reviews. The manufacturer as the expert for the device and related technology is required to know or determine the risks and benefits of its device and technology. A

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<sup>21</sup> 21 CFR § 820; 21 CFR § 820.30

manufacturer with adequate QS SOP in place is assumed by FDA to have sufficient expertise and knowledge to be able to develop its own methods for ensuring that the design input requirements are appropriate for its device to ensure its proposed modified device will continue to meet its same intended use, the needs of the user and remain safe and effective. The FDA's requirements for QS would have each manufacturer continually engaged in quality assurance practices for refining its own device design requirements as verification and validation is obtained about the products' risks and benefits from the manufacturer's trending, quality documents, medical literature, Corrective Actions and Preventive Actions (CAPA) and other reports from its post-market surveillance and complaint handling, reporting and the history of similar products. The manufacturer, not the FDA, must also establish and maintain procedures for defining and documenting design output in terms allowing evaluation of conformance to design input requirements.

43. A manufacturer's QS practices are not reviewed by FDA during its review of the pre-market 510(k) submissions. FDA engages with the post-market commercial device at time of a facility inspection. FDA inspects to look at a "quick overview" of QS procedures that are in place. At that time, the FDA looks at samples of QS to determine if there is a suggestion of larger systemic issues with QS. The FDA then communicates its concerns, if there are any, to Executive Management to address.

## **VI. FDA's actions with IVC filters and the IVC filter industry to protect public health**

### **A. November 1999: FDA issued guidance for cardiovascular intravascular filter 510(k)s.**

44. On November 26, 1999, FDA's Division of Cardiovascular and Respiratory Devices, Office of Device Evaluation (ODE) issued a draft "Guidance for Industry and FDA Reviewers and Staff" ("1999 Guidance") proposing reclassification of IVC filters from clearance as Class III 510(k)s based on support of substantial equivalence to pre-1976 Pre-Amendments Cardiovascular Intravascular Filter predicates to Class II devices with special controls and able to be cleared by Class II 510(k)s.<sup>22</sup> The 1999 Guidance was intended to describe a means by which cardiovascular intravascular filter devices could be shown to comply with a requirement for special controls for clearance of Class II devices. The 1999 Guidance was applicable to the 510(k)s submitted by Bard indicating to the FDA that the performance of its family of Recovery Filters was substantially equivalent to the performance of the SNF predicate device when implanted permanently in a patient.
45. The 1999 Guidance was designated by FDA as a "special control" which required filter manufacturers attempting to establish their new device as substantially equivalent to a predicate cardiovascular intravascular filter to demonstrate in a 510(k) submission that the proposed filter

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<sup>22</sup> Guidance for Industry and FDA Reviewers/Staff Guidance for Cardiovascular Intravascular Filter 510(k) Submissions issued November 26, 1999. The 1999 Guidance superseded FDA's Guidance for the Submission of 510(k) Premarket Notifications for Cardiovascular Intravascular Filters issued February 11, 1997.

device complied with either the specific recommendations of the 1999 Guidance or some alternate control capable of providing equivalent assurances of safety and effectiveness.

46. The 1999 Guidance addressed only filters permanently implanted in the IVC to prevent thromboemboli (clot) generated in the lower limbs from flowing into the right side of the heart and the pulmonary circulation. It is limited “in scope to those filters that are designed in such a way as to be seated within the vena cava via a series of hooks which are at the end of several legs or struts which converge at an apex.”<sup>23</sup> The FDA indicated that filters with a design which significantly differed “may require premarket approval and submission of a premarket approval application (PMA) or a completed product development protocol (PDP).”<sup>24</sup>
47. According to the FDA, for patients in which anticoagulation is ineffective, contraindicated, or results in complications which required anticoagulant discontinuation, “vena caval interruption with a filter is recommended with the goal to try to obtain high filtering efficacy (large and small emboli) without impedance of blood flow and with reduced device related thrombosis while minimizing the risks of migration and without penetration of the vessel wall.”<sup>25</sup> The 1999 Guidance and reclassification of devices to Class II to permit clearance by Class II 510(k)s was further restricted by FDA to IVC filters indicated for use for prevention of recurrent pulmonary embolism via placement of the IVC filter in the vena cava.
48. The 1999 Guidance emphasized the limited use of IVC filters to specific indications for use. The FDA informed all IVC filter manufacturers selling permanent IVC filters after 1999 that they needed to update their labeling and marketing to reflect only the following four cleared indications for use (per Morales (2013)):
  - Pulmonary thromboembolism when anticoagulants are contraindicated
  - Failure of anticoagulant therapy in thromboembolic diseases
  - Emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced
  - Chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated.<sup>26</sup>

These four indications remain the cleared indications for marketing of IVC Filters by the filter industry to the present day.
49. FDA also stated that “manufacturers who wish to pursue other indications should contact FDA to determine the data necessary to support a new indication and the appropriate regulatory pathway.”<sup>27</sup>
50. Therefore, the 1999 Guidance fully described the intended use for IVC filters that could be cleared for marketing as Class II IVC filters. The Guidance’s recommendations were not considered binding for industry but was provided to industry as FDA’s current thinking on the

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<sup>23</sup> *Id.*

<sup>24</sup> *Id.*

<sup>25</sup> *Id.*

<sup>26</sup> *Id.*

<sup>27</sup> *Id.*

topic. Alternative approaches for supporting clearance of 510(k)s could also be proposed and used if the manufacturer's approach satisfied the requirement of the applicable statute or regulations.<sup>28</sup>

51. The 1999 Guidance required that biocompatibility testing should be conducted in accord with ISO-10993 Biological Evaluation of Medical Devices Part 1: Evaluation and Testing. FDA considered cardiovascular intravascular filters as "permanent implant, blood-contacting devices."<sup>29</sup> The 1999 Guidance gave the criteria for an "ideal filter":

- Nonthrombogenic
- High filter efficiency without impedance of blood flow
- Secure fixation within the vena cava
- Rapid and safe percutaneous insertion
- Low rate of associated morbidity
- Magnetic Resonance Imaging (MRI) compatibility.<sup>30</sup>

52. Regarding the testing for manufactures to provide to FDA in the 510(k) submissions for submission as well as the manufacturer's own new IVC filter product development, the 1999 Guidance "may not reflect the complete battery of pre-clinical testing necessary to qualify all filters/designs." FDA continued to describe IVC filter testing for industry and for a 510(k) submission for FDA in terms of the similarity of proposed filter to currently marketed filters:

*However, there are certain aspects of filter design that are general in nature and should be assessed. The degrees to which a proposed device is similar to a currently marketed filter will indicate the level of testing necessary, i.e., whether the design characteristics can be assessed via in vitro bench testing, in vivo animal testing, clinical testing or some combination of all three.<sup>31</sup>*

53. The 1999 Guidance also provided an outline of general issues that need to be addressed by the sponsor when seeking premarket 510(k) clearance of an IVC filter:

*It is the submitter's responsibility to conduct testing which adequately addressed the concerns outlined below as well as any others which may arise due to the unique design of the given device...Test protocols and acceptance criteria for these tests are the responsibility of the submitter.*

*All tests should be performed on filters fabricated by representative manufacturing processes. An adequate number of samples should be tested...The performance specifications, test conditions and acceptance criteria for all tests should be completely explained and justified by comparison to expected clinical conditions. Where appropriate, testing should be conducted in an environment stimulating clinical conditions...*

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<sup>28</sup> *Id.*

<sup>29</sup> *Id.*

<sup>30</sup> *Id.*

<sup>31</sup> *Id.*

54. The 1999 Guidance then provided headings for different areas of pre-market clinical testing that a manufacturer would be expected to complete:
- Simulated deployment
  - Introducer/Sheath suitability
  - Clot trapping ability<sup>32</sup>
  - Filter fracture<sup>33</sup>
  - Caval perforation/filter migration<sup>34</sup>
  - Thrombogenicity<sup>35</sup>
  - MRI Compatibility<sup>36</sup>
55. Regarding “Clinical Investigations,” the FDA wrote that “it is anticipated that human clinical investigations could be necessary in the development of a “new” vena cava filter to establish equivalency to currently marketed filters. For indications already used for 510(k) clearance of IVC filters, the risks and benefits to patients were well-documented. Therefore, the intent of clinical studies for those indications should be used to demonstrate that the rates of complications for the investigational filter are comparable to other marketed vena cava filters.
56. The 1999 Guidance was not intended to address the testing necessary to develop and support clearance for a new intended patient population or indication for use for permanent IVC filters, only a new design. There was no predicate IVC filter cleared post-1999 for a new prophylactic indication or implantation of filters in patients able to take adequate anticoagulant therapy. The Guidance did not address IVC filters implanted in women during pregnancy or patients undergoing elective surgical procedures like bariatric and joint replacement surgery. Nor did the Guidance address IVC filters intended for retrieval. Those are all significant new indications for implanting IVC filters not shared by pre-1976 predicate devices or post-1976 cleared predicates. Therefore, for Bard or any other filter manufacturer to obtain new indications for legal marketing of an IVC Filter would first require them to provide the FDA with scientific evidence capable of supporting the safety and efficacy of an IVC filter for the new indication before any marketing.

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<sup>32</sup> FDA described methods for “clot trapping” as able to demonstrate the filter captured clinically significant emboli yet still permit sufficient blood flow around the trapped emboli without producing caval occlusion.

<sup>33</sup> FDA described “filter fracture” as the filter’s response to worst-case respiratory and diaphragmatic movements in the vena cava under simulated respiratory cycles should demonstrate sufficient fatigue resistance of the filter design. In addition, there should be an examination of corrosion resistance and weld strength following cycling.

<sup>34</sup> The FDA described “caval perforation/filter migration” as testing to demonstrate that the filter fixes itself within the vena cava at the deployment site and undergoes sufficient endothelialization. The force necessary for device fixation should be characterized over the range of labeled inferior vena cava (IVC) diameters. In addition, this fixation force should not suggest a tendency for the device to perforate the caval wall.

<sup>35</sup> FDA’s description of “thrombogenicity” was testing to demonstrate the effect of the device on blood flow should not be sufficient to cause blood stasis, which could lead to thrombus (clot) formation in and around the device.

<sup>36</sup> 1999 Guidance

The FDA would then decide the appropriate regulatory route to market whether a PMA, completion of a product development protocol (PDP), or clearance using the 510(k) process.

57. The 1999 Guidance provided that in clinical investigation of new filter designs, all patients dying in the manufacture's clinical study should have autopsies with a complete report of findings provided to FDA for review. Deaths from filter complications had been reported from:

- Cardiac arrest immediately after filter placement
- Misplacement of the filter during insertion
- Cephalic migration of a filter to the heart after placement.<sup>37</sup>

58. The 1999 Guidance listed the following headings for providing clinical data to the FDA for obtaining clearance of a 510(k) for a permanent IVC filter and the standard indications for prevention of PE recurrence:

- Complications during filter insertion
- Recurrent Pulmonary Embolism
- Death
- Filter Migration
- Caval penetration
- Filter tilting and angulation
- Caval occlusion
- Filter embolization
- Other Risks.

59. For "Filter Migration" the FDA wrote that minor filter migration in the caudal and cephalic direction is commonly reported. The FDA stated, "[t]he walls of the vena cava are known to move with respiration and changes in intra-abdominal pressure induce flexion on the limbs of the filter." The Guidance also described the known causes of migration:

*True migration may be caused by an excessively large vena cava, inadequate positioning and massive embolization into the filter with caval dilatation. It is recommended that any movement of the filter with relation to the spine that is 5mm or greater be recorded as filter migration. Assessment of distal migration should be determined from post implant and follow-up anterior-posterior and lateral films after correction for magnification. . . .*<sup>38</sup>

60. In "Caval penetration" the FDA indicated that on CT scans:

*[A]n increase in filter base diameter of  $\geq 5$ mm is recorded, a CT scan should be performed to confirm or exclude the position of filter legs outside the inferior vena cava. Any other changes, which may be suggestive of possible*

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<sup>37</sup> *Id.*

<sup>38</sup> *Id.*

*filter leg penetration of the vena cava, should trigger a CT scan, regardless of increase in the filter base diameter.*<sup>39</sup>

61. Under “Filter tilting and angulation” FDA wrote for industry and reviewers:

*The significance of tilting of caval filter after placement is controversial. There is a theoretical loss of filtering efficacy of any filter when tilted or angulated significantly...All instances of tilting or angulation should be noted as well as any associated clinical sequelae.*<sup>40</sup>

62. For “Caval occlusion” the FDA indicated the problem was:

*related to filter thrombogenicity, design and flow patterns....Since it is often clinically difficult or impossible to distinguish IVC filter occlusion from extension of the preexisting DVT because the symptoms may be similar, all instances should be recorded as occlusion unless the extension of DVT can be ruled out.*<sup>41</sup>

63. The discussion of “Filter Embolization” reflected the prior history of permanently implanted IVC filters through November 1999:

*The risk of filter embolization is primarily limited to the first two weeks after implantation. Embolization of the filter is a serious complication with variable clinical consequences, comparable to pulmonary thromboembolism. These range from being totally asymptomatic to sudden death. Therapy ranges from no therapy to open chest surgery and removal of the device. All cases of filter embolization should be recorded and the reasons for the occurrence immediately assessed. The subsequent treatment should also be described in detail.*<sup>42</sup>

64. The 1999 Guidance ended with a set of label update recommendations which should be voluntarily incorporated in the labeling and marketing based on FDA’s review of current (1999) IVC filter labels. The updated information was to ensure consistency among IVC filter manufacturers’ labels and to facilitate appropriate use by physicians clinically. The label sections recommended by ODE included: 1) Indications for use<sup>43</sup>; 2) Contraindications; and 3) Warnings

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<sup>39</sup> *Id.*

<sup>40</sup> *Id.*

<sup>41</sup> *Id.*

<sup>42</sup> *Id.*

<sup>43</sup> Indications for Use:

- 1) Pulmonary thromboembolism when anticoagulants are contraindicated
- 2) Failure of anticoagulant therapy in thromboembolic diseases
- 3) Emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced
- 4) Chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated.

which added MRI compatibility information for the metal in the filter and stability of the filter in the patient when placed into a magnetic field environment such as MRI. For Contraindications, FDA indicated that the labeling “may include other contraindications which are specific to your particular device design.”<sup>44</sup>

65. Bard as a 510(k) applicant to market a family of Recovery Filters and an expert in devices intended to be permanently implanted in patients, had a duty to be aware of all of the information contained in the FDA’s 1999 Guidance. That would have included the FDA’s description of IVC filter risks and indications for use, which Bard was required to follow in its marketing of its IVC filters.

### **Part 870-CARDIOVASCULAR DEVICES**

#### **Subpart D- Cardiovascular Prosthetic Devices**

#### *21 CFR§ 870.3375 Cardiovascular intravascular filter.*

(a) *Identification.* A cardiovascular intravascular filter is an implant that is placed in the inferior vena cava for the purpose of preventing pulmonary thromboemboli (blood clots generated in the lower limbs and broken loose into the blood stream) from flowing into the right side of the heart and the pulmonary circulation.

(b) *Classification.* Class II. The special controls for this device are:

(1) “Use of International Standard’s Organization’s ISO 10993 Biological Evaluation of Medical Devices Part I: Evaluation and Testing,” and

(2) FDA’s:

(i) 510(k) Sterility Review Guidance and Revision of 2/12/90 (K90-1)” and

(ii) Guidance for Cardiovascular Intravascular Filter 510(k) Submissions.”<sup>45</sup>

### **B. August 9, 2010: The FDA issued an initial safety communication regarding removal of retrievable IVC filters.**

66. On August 9, 2010, the FDA issues a Safety Communication regarding the removal of retrievable IVC filters.<sup>46</sup> The FDA’s communication was intended for implanting physicians as well as clinicians providing ongoing care to patients implanted with IVCs.
67. The FDA had seen the annual use of IVCF filters rapidly increase over the last 30 years. In 1979, 2,000 IVCF were implanted, in 2007 almost 167,000, and it was projected that by 2012 259,000. However, since 2005, FDA has received 921 IVCF adverse event reports, 328 involved migration ( $\pm$ %), 146 embolizations (detachment of device components) (16%), 70 reports of perforation (8%) and 56 involving device fracture (6%). The FDA continued that it was associating the

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<sup>44</sup> 1999 Guidance.

<sup>45</sup> CFR Title 21 (current through April 1, 2016), *available at* <http://www.fda.gov>

<sup>46</sup> FDA Safety Communication August 9, 2010 *Removing Retrievable Inferior Vena Cava Filters: Initial Communication*, *available at* <http://www.fda.gov/MedicalDevices/Safety/AlertsNotifications/ucm221676.htm>

adverse events with failure of physicians to remove the retrievable IVC filters were no longer necessary for protection against PE:

*These types of events may be related to retrievable filter remaining in the body for long periods of time, beyond when the risk of PE has subsided.*

*The FDA is concerned that these retrievable IVC filters, intended for short-term placement are not always removed once a patient's risk of PE subsides. Known long-term risks associated with IVC filters include but are not limited to lower limb deep vein thrombosis (DVT), filter fracture, filter migration, filter embolization and IVC perforation.*

**Recommendations/Actions:**

**FDA recommends that implanting physicians and clinicians responsible for the ongoing care of patients with retrievable IVC filters consider removing the filter as soon as protection from PE is no longer needed.**

**FDA Activities:**

*More information about FDA's decision analysis model including risks/benefit implantation timeframe suggestions will be made available in an update to this communication...<sup>47</sup>*

**C. 2013: FDA's publication of its analysis and recommendation for early removal of retrievable IVCFS**

68. As the FDA discussed in its August 2010 Communication to healthcare providers, in 2013 it published its findings from its review of retrievable IVC filters. Morales (2013)<sup>48</sup> was the FDA's published review of patients with transient, reversible risk of PE had passed. The FDA's quantitative decision analysis suggested that the benefit/risk profile begins to favor filter removal between 29 and 54 days after implantation.<sup>49</sup>
69. The FDA in Morales (2013) also addressed both the on-label (cleared) and off-label (not-cleared) prophylactic use of IVC Filters:

The use of inferior vena cava (IVC) filters in patients without a history of pulmonary embolism (PE), commonly referred to as a *prophylactic use*, is considered off-label use if the device because it lies outside of

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<sup>47</sup> *Id.*

<sup>48</sup> Morales JP et al., Decision analysis of retrievable interior vena cava filters in patients without pulmonary embolism, *Jour Vasc Surg: Venous & Lymph Dis.*, 2013 Vol 1, No.4. at 376-84 (FDA's published review recommending removal 29 to 54 days after the transient risk of PE has passed) [hereinafter "Morales (2013)"].

<sup>49</sup> *Id.*

the indications for use that the U.S. Food and Drug Administration (FDA) has cleared for these devices. Currently, all IVC filters on the market in the United States have the following indications for use, which the FDA believes is appropriate based on the clinical data supporting their use: “for the prevention of recurrent pulmonary embolism (PE) via placement in the vena cava in the following conditions”:

- Pulmonary thromboembolism when anticoagulants are contraindicated
- Failure of anticoagulant therapy in thromboembolic diseases
- Emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced
- Chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated.<sup>50</sup>

70. FDA continued that it has cleared all retrievable IVC Filters as permanent IVC Filters as well. All retrievable filters have been cleared with the statement: “The filter may be retrieved in patients who no longer require a filter.” FDA reiterated, “Any use outside the (above) FDA-labeled indications is considered off-label use of the device.”

71. FDA indicated that multiple factors have driven the use of temporary filters in patients. However, FDA considered there to be significant limitations in the studies of patients for this indication, making the statement that the “benefit/risk balance of this off-label IVC filter implantation is a patient without a history of PE is unclear.” The off-label use of IVC filters in the United States was believed by FDA to account for more than 50% implanted, with 50% or fewer of the filters removed. The risk of a complication from the implanted would be expected to increase with the duration of implantation, “as with any chronic implant.” FDA continued that “this raises safety concerns for patients who received IVC filters with the expectation that implantation would be temporary but whose filters are not removed when the need for filtration is subsided.”

This practice of leaving retrievable IVC filters in situ that could be removed could be due to a lack of data identifying appropriate retrieval times, loss of follow-up of patients, or lack of physician initiative to consider device retrieval....

Since it is beyond the FDA’s mission to regulate the practice of medicine, including the prophylactic use of IVC filters, the main focus of the decision analysis model was to assess the risk/benefit profile of the IVC filter use over the potential life of the implant. Emphasis was placed on the off-label prophylactic use of these devices once they had already been implanted per clinician judgement (e.g., as part of trauma care or bariatric and orthopedic surgery).

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<sup>50</sup> *Id.*; 1999 Guidance.

...If the patient's transient risk of PE has passed, the risk-benefit profile resulting from the analysis begins to favor filter removal between 1 to 2 months, assuming retrieval is possible.<sup>51</sup>

72. The FDA does not have a role to become directly involved in the day-to-day patient-physician treatment relationship. However, based on its own analysis it provided guidance that the retrievable filters should be retrieved when the clinical need was gone.

**D. May 6, 2014: The FDA's updated safety communication recommends removing retrievable IVC filters and requires post market surveillance studies from the IVCF industry.**

73. The FDA on May 6, 2014, issued a Communication encouraging the removal of retrievable IVC filters when feasible. The FDA Communication was based on recently published research and post market studies for the devices. FDA said that reports also included difficulty with removal of the retrievable filters. FDA described the reports it had received of

*device migration, filter fracture, embolization (movement of the entire filter or fracture fragments to the heart or lungs), perforation of the IVC, and difficulty removing the device. Some of these events led to adverse clinical outcomes. The types of events may be related to how long the filter has been implanted....For patients with retrievable filters, some complications may be avoided if the filter can be removed once the risk of pulmonary embolism has subsided...*<sup>52</sup>

74. FDA announced the Morales (2013) publication and that it was downloadable from the FDA. The conclusion had been that for implanted patient after a transient risk of PE had passed, the risk/benefit profile developed by FDA began to favor removal of the filter between 29 and 54 days after implantation. FDA also announced that it was requiring collection of additional clinical data for currently marketed IVC filters in the United States from manufacturers. The data was to be collected to address safety questions that remain unanswered for both permanent and retrievable IVC filters. Manufacturers were given two options by FDA for obtaining clinical performance data: 1) Participate in the PRESERVE<sup>53</sup> (Predicting the Safety and Effectiveness of Inferior Vena Cava Filters) study, an independent national clinical study looking at the outcome of filters of participants; or, 2) pursuant to responding to FDA's 522 Order,<sup>54</sup> conduct a post

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<sup>51</sup> Morales (2013)

<sup>52</sup> May 6, 2014 FDA Safety Communication Removing Retrievable Inferior Vena Cava Filters, *available at* <http://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm396377.htm> [hereinafter "May 2014 Safety Communication"]

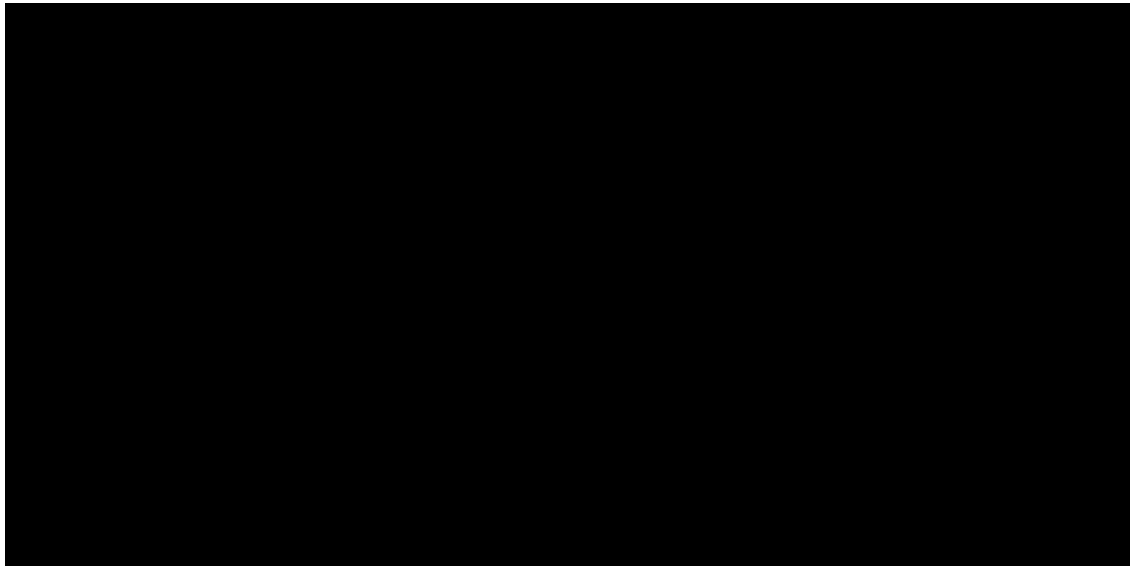
<sup>53</sup> PRESERVE Study

<sup>54</sup> FDA 522 Order-Studies mandated under Section 522 of the FDCA- 522 Postmarket Surveillance Studies program encompasses design, tracking, oversight and review responsibilities for studies mandated to be conducted under Section 522. See Postmarket Surveillance Under Section 522 of the Federal Food, Drug and Cosmetic Act Guidance for

market surveillance study of their filters. The post market performance data gathered from the PRESERVE Study and the individual 522 studies would hopefully be able to contribute to the FDA's, manufacturers', and health care professional' knowledge and ability to assess the safety profile of the commercial devices, their intended use, the evolving patterns of clinical use, and the label to improve patient care.<sup>55</sup>

75. According to the FDA's Guidance of Postmarket Surveillance under Section 522, Section 522 of the FDCA provided the FDA with the authority to require manufacturers to conduct post market surveillance of certain Class II or Class III devices. Postmarket surveillance however, was not to be viewed as a substitute for the sponsor obtaining the necessary premarket information to support 510(k) clearance or PMA approval.
76. Failure of a manufacturer to comply with the requirements of the issued section 522 Order is a Prohibited Act (21 USC§ 331(q)(1)( C) and renders a device misbranded under 21 USC §352(t)(3) which can lead to other FDA enforcement actions including seizure, injunction, prosecution and /or civil penalties. Manufacturers are able to request an exemption from the requirements to conduct post market surveillance to obtain post market safety information, which FDA can consider under 21 CFR §822.30. However, the 522 Order once issued is to be complied with even if a manufacturer stops marketing the device. However, FDA considers requests to terminate, modify or use alternative methods for obtaining post market safety data, for example Bard's participation in the PRESERVE study, on a case-by-case basis. (21 CFR§ 822.28)

**VII. BASES FOR OPINION #1: BARD'S PREMARKET ACTIONS WITH DESIGN AND DEVELOPMENT OF THE RNF AS A PERMANENT IVC FILTER WERE INADEQUATE**



Industry and Food and Drug Administration Staff was issued April 27, 2006, August 16, 2011 and May 16, 2016  
([www.fda.gov/downloads/medicaldevices/DeviceregulationandGuidance/GuidanceDocuments/ucm268141.pdf](http://www.fda.gov/downloads/medicaldevices/DeviceregulationandGuidance/GuidanceDocuments/ucm268141.pdf))

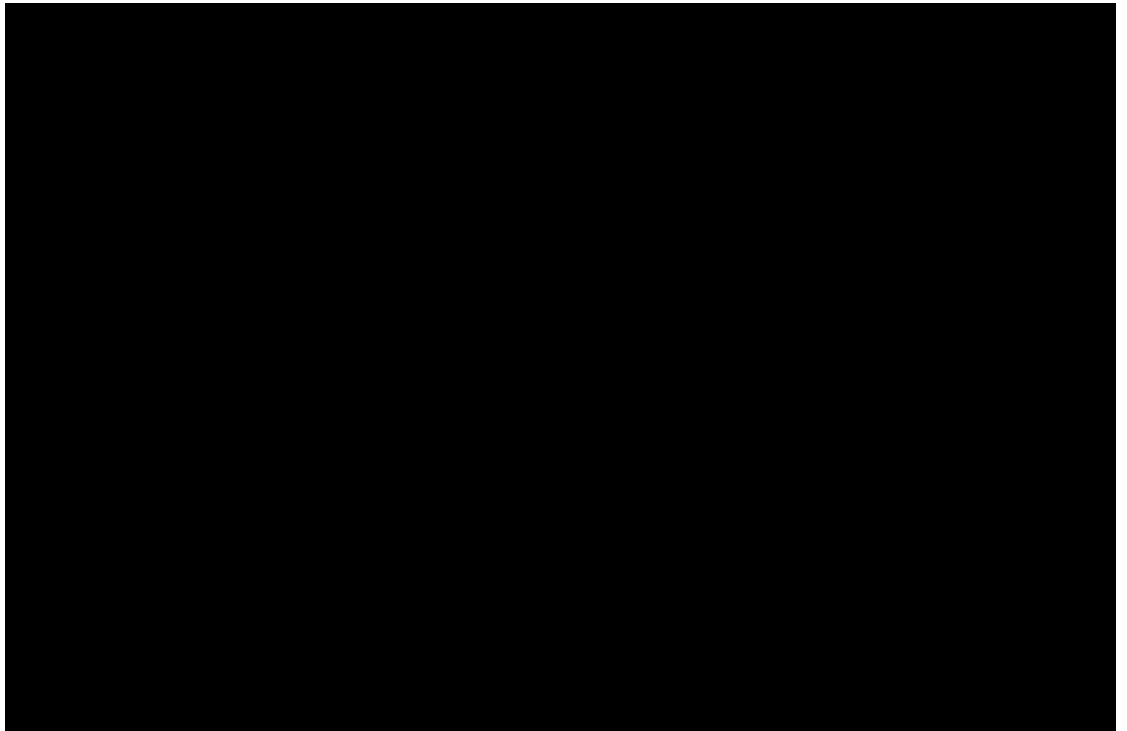
<sup>55</sup> May 2014 Safety Communication



***Applicable Regulations:*** 21 CFR § 807; 21 CFR § 860; 21 CFR § 820; 21 CFR § 806; 21 CFR § 801.109; 21 USC § 331(a)(b); 21 USC § 352(a)(f)(1)(2),(t); 21 USC § 321(n); 21 USC § 351

The following are examples of information Bard had prior to 510(k) clearance which should have supported that the SNF and RNF were not substantially equivalent in terms of implanted in patients as permanent implants:

- Dr. Asch's Pilot Study human data with RNF beginning April 2000 with reports of filter tilting, migration, caval perforation, and fracture



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<sup>56</sup> BPV-17-01-00019382

<sup>57</sup> BPV-17-01-00084073

<sup>58</sup> BPV-17-01-00002650

<sup>59</sup> BPV-17-01-00067972; BPV-17-01-00072740

<sup>60</sup> BPV-17-01-00067972

<sup>61</sup> BPV-17-01-00034448

<sup>62</sup> BPV-17-01-00058992

<sup>63</sup> BPVE-01-00066044; BPVE-01-00280772

<sup>64</sup> BPVE-01-00280772

<sup>65</sup> BPVE-01-01351166



All this information available to Bard prior to obtaining 510(k) clearance from the FDA as a permanent filter, including first-hand knowledge of the history of performance of the SNF predicate device as well as its superior efficacy in clot trapping, should have alerted a responsible medical device manufacturer to evaluate the adequacy of the RNF design prior to starting commercial sales. Even when released with a minimum 50mmHg migration resistance, as was quickly shown in the Dr. Asch study the RNF had less resistance to than the SNF motion in the IVC when implanted short-term in a patient. This raised new issues of safety and efficacy which Bard was required to address before it could legally market and sell the device to the public.

**A. The predicate: the Simon Nitinol Filter (SNF) was a clinically successful permanent IVC filter.**

**1. 1984: The SNF's United States patent described "known risks" for IVC filters for "migration, fracture, tilt, perforation."**

77. Dr. Morris Simon<sup>69</sup> is the inventor of the Simon Nitinol "Blood Clot Filter." The Simon Nitinol Filter (SNF) was used by Bard as the "predicate device" (i.e., the "gold standard") to support safety and efficacy for Bard's 510(k) Recovery Filter (RNF) clearance. Bard claimed the RNF family of filters (Recovery, G2, G2X, Eclipse, Meridian, Denali) were all substantially equivalent to SNF when implanted as a permanent IVC filter. Therefore, a key to understanding differences between SNF (the predicate) and Bard's RNF and the relation to the 510(k) clearance can be seen in US Patent statements and diagrams. Another benefit of the US Patents is the BACKGROUND provided by Dr. Simon as a snapshot of IVC Greenfield Filter option, another permanent predicate IVC filter cited by Bard. All the devices are implanted as an alternative to surgery or

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<sup>66</sup> Fuller Exhibit 127 K022236

<sup>67</sup> BPV-17-01-00058778

<sup>68</sup> BPV-17-01-00002650

<sup>69</sup> Dr. Morris Simon was a professor at Harvard Medical School that died suddenly and unexpectedly on January 17, 2005 one day after his 79<sup>th</sup> birthday. He worked at the Beth Israel Deaconess Medical Center in the Department of Radiology. He was born in Johannesburg, South Africa in 1926. After medical school, he did training in radiology in London in 1951. He conceived of using Nitinol for an IVC filter. The SNF has subsequently been modified into stents and closure devices for atrial septal defects.

anticoagulants in patients at known risk of excess clotting to help reduce risk of pulmonary embolism (PE).

78. The SNF, developed by Dr. Simon as with other IVC filters was viewed as an alternative to use of anticoagulants or surgery or both in patients at known risk for excess clotting risk. He indicated one treatment for a patient at known risk of pulmonary embolus (PE) recurrence was surgery: the “vena cava has been traditionally tied (ligated) or its cross-section has been subdivided using sutures or clips to reduce the risk of pulmonary emboli from reaching the patient’s lungs through the inferior vena cava”<sup>70</sup>. He continued that “more recently the vena cava has been interrupted by inserting into the vena cava a filtering or obstructing device indirectly via remote but more accessible vein, such as the jugular vein in the neck or the femoral vein in the groin.”<sup>71</sup> He called the insertion process for these devices as “complex, time consuming, and sometimes associated with surgical complications at the insertion site, with the risk of introduction of an air embolism and hemorrhage.”<sup>72</sup>
79. Dr. Simon was a physician, radiologist, professor at Harvard Medical School and an early pioneer in Interventional Radiology (IR). He proposed using a new material Nitinol (nickel and titanium alloy), a thermally activated, lightweight metal with shape memory to create new stents and filters. He was listed as the inventor of the SNF on US Patent No. 4,425,908 filed October 22, 1981 and assigned on January 17, 1984. The assignee for the US Patent was Beth Israel Hospital, Boston, MA. (Harvard University) The Simon 1984 abstract: “...*In the expanded configuration, the filter comprises a plurality of wires in the form of overlapping loops, with portions of the loops contacting the inner wall of the vein, providing a filter basket at the leading end of the filter; at the training end the wires have circumferentially spaced leg portions whose free ends contact the inner wall of the vein. The filter wires are composed of a material having a first, relatively pliable low-temperature condition and a second, relatively rigid high-temperature condition.... Upon emerging from the catheter, the filter responds to the ambient temperature and assumes its functional form.*”<sup>73</sup>
80. Dr. Simon provided a diagram of his proposed Simon Nitinol Filter. His design included an upper wide nest-like (petal-like) section intended to push out against the vessel wall to anchor and help stabilize the device in the blood flow of the inferior vena cava (IVC). There was a distinct lower section of legs intended to catch emboli (basket), as well as featuring attachment hooks to further anchor the device in the blood stream of the vena cava. The design had features included in both sections to help counteract (counterbalance) forces placed on the filter in the patient’s IVC and blood flow to help reduce the risk of migration in any of the two longitudinal directions (up and down). The goal of the SNF design was to improve filter stability when permanently implanted in a living and moving patient.

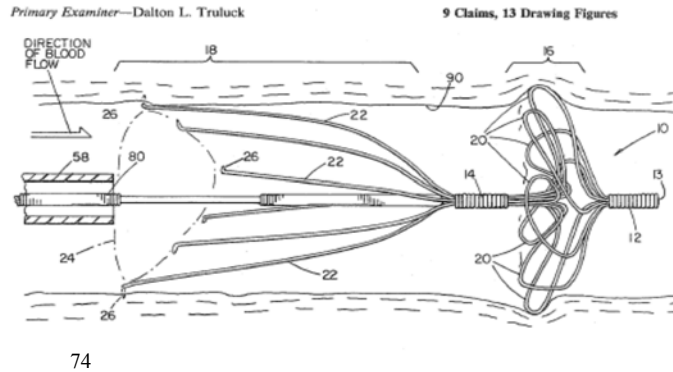
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<sup>70</sup> US Patent No. 4,425,908 filed October 22, 1981 and assigned January 17, 1984 for the “Simon Nitinol Filter”

<sup>71</sup> *Id.*

<sup>72</sup> *Id.*

<sup>73</sup> *Id.*



81. The 1984 Simon US Patent provided a discussion of other available IVC filter technology and known risks for similar devices parenterally inserted by imaging. He described the 1) Mobin-Uddin Umbrella, and 2) Kimmell-Greenfield Filter. Like the SNF, the devices were inserted via the internal jugular vein (IJ) (neck) or the femoral vein (groin).
82. Dr. Simon's SNF was intended to be implanted permanently in a patient that could not be anticoagulated and at known risk of embolism and death. There was no proposal by Dr. Simon in his 1984 US Patent to insert the SNF *prophylactically* (temporarily) in a new group of patients.
83. The 1981 Simon application (the patent application was in 1981 although it was not assigned until 1984) indicated that a goal of the new Nitinol device was for the filter to remain "firmly attached to the vein," "not tend to cause other complications" and "retain all potentially dangerous emboli" (bolding added for emphasis):

*a filter than can be **firmly attached to the vein**, that is not easily dislodged, that does not tend to become totally obstructed by retained emboli, that does not tend to cause thrombosis, leg edema or other complications and that retains all potentially dangerous emboli.*

**a. One Alternative Available Permanent IVC Filter: Modin-Uddin Umbrella<sup>75</sup>**

84. The Modin-Uddin Umbrella (US Patent No 3,540,431, issued Nov 17, 1970) even in 1970 had features common to and different from the SNF. The Modin-Uddin was a pre-1976 IVC Filter and it is made of the metal Elgiloy, not Nitinol.
85. The Modin-Uddin US Patent in 1970 described a collapsible device with umbrella-like struts (six radiating spokes), the end of each strut sharpened to anchor/spear/ impale the patient's IVC vessel

<sup>74</sup> *Id.*

<sup>75</sup> 1999 Guidance. FDA proposed to reclassify Cardiovascular Intravascular Filters (including IVC Filters) from Class III pre-Amendments devices requiring clearance of a Class III 510(k) to Class II cleared by 510(k). There was no proposal to include IVC Filters by 510(k) for prophylactic indication.

wall. The device was designed that when deployed and opened (expanded) the leg span would be greater than a “commonly encountered vena cava.” Unlike the later SNF (Nitinol), the Modin-Uddin device was made of a resilient alloy material called “Elgiloy”,<sup>76</sup> a metal developed for wire springs for watches by the Elgin National Watch Company.

86. Dr. Simon described one risk of the Modin-Uddin device was that it “*may be dislodged and migrate towards the heart.*” Another known risk was obstruction of the device and blood flow of the IVC by captured clots “*tends to become totally obstructed even with small amounts of embolus.*” Finally, Dr. Simon said that once implanted the Modin-Uddin Umbrella had a risk for “*perforation of the vena cava wall with local hemorrhage may occur.*” So, tendencies for migration, obstruction and caval wall perforation were already known risks for IVC filters in 1981.

#### **b. Second Alternative Available Permanent IVC Filter: Greenfield Type**

87. Bard’s 510(k) for RNF referenced the titanium Greenfield Filter as the other predicate permanent filter besides SNF for clearance of the RNF. Bard told the FDA that the clot capturing of the RNF was comparable to the titanium Greenfield filter. The Greenfield filter design began as a pre-1976 device.
88. The Kimmell-Greenfield filter US Patent described also a conical umbrella-like filter device made of a resilient wire covered with a synthetic resin material coating. The subsequent commercial Greenfield filters retained the conical shape and have been made of various metals including stainless steel and titanium.
89. The Kimmell-Greenfield IVC Filter comes pre-loaded in its insertion instrument (carrier) (basically a syringe) for use of the physician. The filter was placed under fluoroscopy just like the SNF and Modin-Uddin Umbrella. The physician’s pushing of the carrier’s plunger releases fluid which hydraulically actuated (triggered) the ejector feature of the carrier, pushing the filter off and away from the carrier, releasing it out into the patient’s blood vessel where it can expand. Once the filter was released from the carrier, its legs would automatically spring outwards (open) to assume the device’s intended general cone shaped configuration in the IVC. Unlike the Modin-Uddin umbrella’s spears, the Greenfield filter has “hooks” at the end of the end of each leg (vane) intended to bite into (hook) the blood vessel wall and serve as an anchor for stability.

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<sup>76</sup> Elgiloy is a metal alloy, but is not a “thermally triggered metal” like Nitinol and shape memory. According to Wikipedia, Elgiloy is Cobalt-Chromium-Nickel alloy also containing iron, molybdenum and manganese. It is used for making springs that are corrosion resistant with high strength, “ductility,” and good fatigue life. Elgiloy () following World War II, returning servicemen complained that their Elgin watches couldn’t take punishment of the corrosive environments in the various theaters of war. In response, Elgin National Watch Company, the predecessor of “Elgin Specialty Metals” and its wire division developed Elgiloy Alloy as a non-corroding watch spring material. Today Elgiloy Specialty Metals Wire Division produces more than 40 high performance alloys intended for aerospace, petrochemical applications and medical devices. See Elgiloy website, at <http://www.elgiloy.com>.

The body of each leg also had U-shaped bends made in the metal to help better capture and restrain clots, but still permit blood flow.

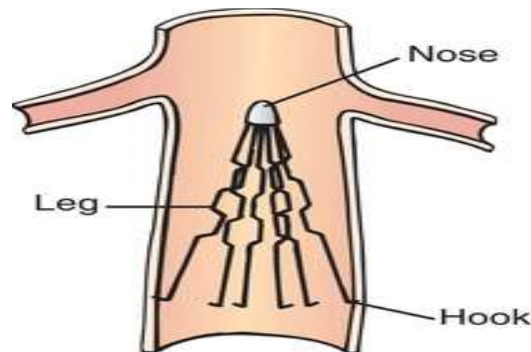
90. For the Kimmell-Greenfield Filter, Dr. Simon indicated a known risk for the Greenfield design was that if the filter tilted backwards or sideways after delivery, it was less effective for capturing and holding on to clots. Dr. Simon described other issues for the Kimmell-Greenfield filter design which he thought helped “reduced effectiveness” (reduce clot capture), namely migration distally, perforate, and tilt when placed in a large vena cava (bolding added for emphasis):

*device may **migrate distally** due to the **water hammer effect of the column of bleed above the filter.***

***Perforation** may occur, sometimes with local hemorrhage*

*Moderate sized emboli may pass through the filter, particularly if **tilted or the vena cava is large.***

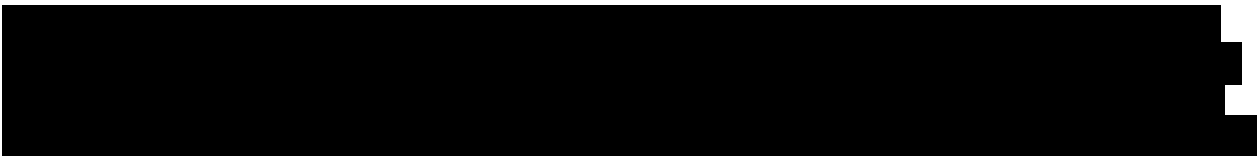
91. Below is a rudimentary diagram of the Kimmell-Greenfield Filter System inserted in the IVC. It shows the U-bends in the legs, the terminal hooks, and convergence point of the legs at the top (nose). These are the characteristic features with generations of Greenfield IVC Filters.



**B. Nitinol Medical Technologies (NMT) obtained multiple 510(k) clearances for the SNF as a permanent IVC filter prior to the FDA’s changes to design requirements.**

92. NMT obtained clearance of several 510(k)s from 1990 through 1997 for sale of the SNF IVC Filter System in the United States. This was a time when FDA’s Good Manufacturing Practices (GMP) (21 CFR 820) did not place as great an emphasis on the manufacturing ensuring adequate design and process controls for creating, production and selling a new medical device. That was changed by the Safe Medical Device Amendments (SMDA) of 1990. After SMDA the FDA’s emphasis and as a result the medical device industry’s design and testing requirements, risk management methods were increased for new products now marketed according to changes for the Good Manufacturing Practices of the Quality Systems Regulations post-1997. There was a greater emphasis placed on the role of the medical device manufacturer to ensure the pre-market

and post-market safety of its medical devices by the FDA's updated Quality Systems Regulations implemented in 1997.

93. NMT was the specification developer and manufacturer identified for the following seven SNF 510(k)s cleared by FDA as permanent IVC Filters. NMT continued to use the SNF as the predicate for each next 510(k) after its initial clearance in 1990:
  - K894703 SNF submitted July 24, 1989 and cleared April 20, 1990;
  - K912144 SNF Modification submitted May 13, 1991 and cleared October 17, 1991;
  - K940489 SNF submitted January 4, 25, 1994 (correspondent Stephen Kleshinski) and cleared August 9, 1994;
  - K944353 SNF/ Straight Line System submitted August 30, 1994 and cleared April 28, 1995;
  - K963016 SNF System submitted August 2, 1996 and cleared November 18, 1996; K963014 SNF/Straight Line System submitted August 2, 1996 and cleared November 18, 1996;
  - K970099 submitted January 10, 1997 and cleared April 15, 1997.
94. The final cleared 510(k) for NMT was April 15, 1997, to market a modification to the SNF delivery system not the filter. The last filter modification 510(k) was cleared August 1994.
95. According to NMT's July 17, 1997, Technical File Design Dossier for marketing SNF/Straight Line System in Europe, NMT created the design specifications but did not actually make or test the lots of SNF System components.<sup>77</sup> NMT subcontracted out component manufacturing, finished device sterilization and testing. NMT developed the design specifications. NMT performed the final packaging and assembly functions. All the SNF products sold and distributed in the EU were by Bard LTD. and in the United States after 1992 by Bard. The SNF/SL was sold for insertion by femoral, jugular/subclavian and also antecubital (arm) routes since cleared in 1995 by K944353, with international sales starting in 1996.
96. In terms of manufacturing and GMP/ Quality Systems, all produced SNF filters were subject to routine Quality Control lot release testing per the subcontractor's specifications. All (100%) received SNF by NMT then underwent an additional inspection via NMT's procedure IP-0004. Each received product must be able to pass this inspection prior to NMT's release of the components for final assembly as finished devices. All incoming inspection data for each lot of filters was received and kept at NMT's Quality Assurance Department.<sup>78</sup>
97. 

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<sup>77</sup> BPVE-01-00066044

<sup>78</sup> BPVE-01-00066044

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100.

101.

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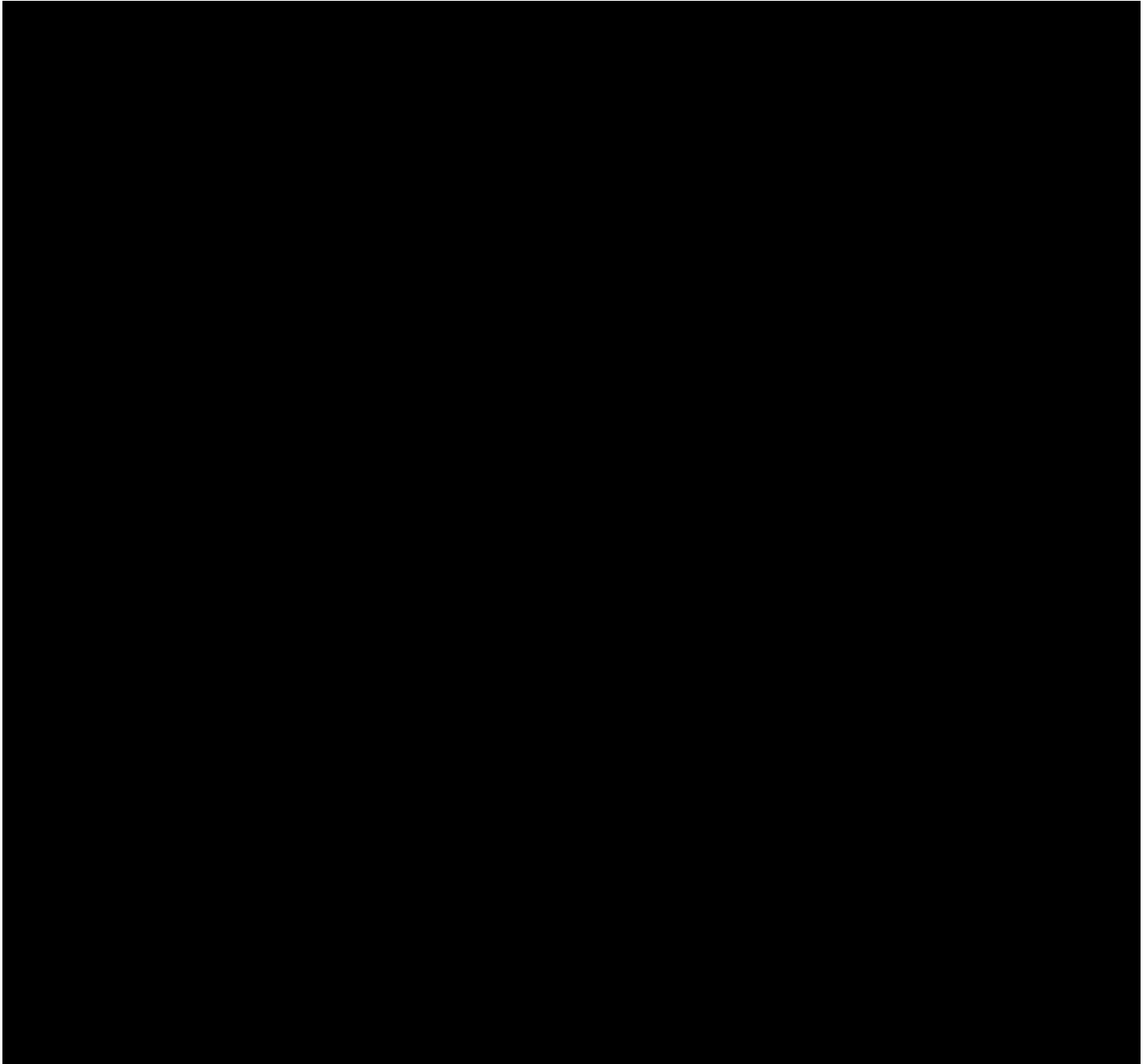
<sup>79</sup> BPVE-01-00066044

<sup>80</sup> BPVE-01-00066044

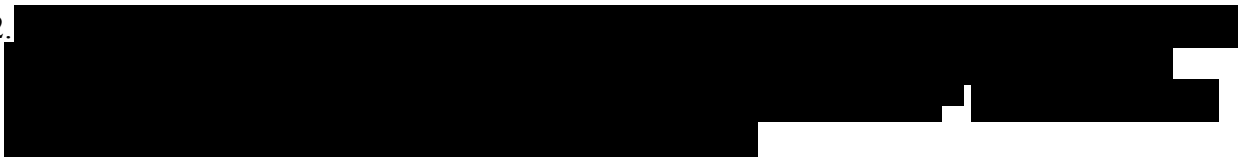
<sup>81</sup> Prince MR, et al., Local intravascular effects of Nitinol wire blood clot filter. *Invest. Radiol.* Apr. 1988, 23(4), at 294-300

<sup>82</sup> ASTM G61-86, Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements for Localized Corrosion Susceptibility of Iron-, Nickel-, or Cobalt-Based Alloys.

<sup>83</sup> BPVE-01-00280772



102.



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<sup>84</sup> BPVE-01-00066044

<sup>85</sup> Simon Nitinol Filter/Straight Line System TECHNICAL FILE July 17, 1997 BPVE-01-00066044 at 66099

<sup>86</sup> BPVE-01-00280772

[REDACTED]

103. [REDACTED]

104. [REDACTED]

[REDACTED]

**C. When NMT transferred SNF production in-house, it updated the SNF specification for release.**

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<sup>87</sup> BPVE-01-00280772

<sup>88</sup> McCowen T, et al, Complications of the Nitinol Vena Cava Filter, *JVIR* 1992, Vol 3. No. 2, at 401-408

<sup>89</sup> BPVE-01-00280772

<sup>90</sup> BPVE-01-00280772

105. All of NMT's SNF device 510(k)s were cleared before 1998 in a significantly different FDA regulatory environment than would face NMT's Recovery IVC Filter in 2000 and Bard's Recovery IVC Filter 510(k)s in 2002 and 2003. The differences are best shown by the June 2001 transfer of SNF manufacturing to in-house at NMT from its contractor Lake Regional Manufacturing, Inc. (LRM) Chaska, MN. The source of the Nitinol material would remain the same. LRM had produced SNF per NMT's general filter specification as described in its US Patent and cleared in its 510(k)s. NMT would inspect LRM-produced SNF filters for acceptance before NMT began final assembly, packaging and sterilization to release the final commercial product it sent to Bard. This relationship between NMT and LRM had resulted in a successful commercial and clinical history of SNF starting in the early 1990s. However, to transfer manufacturing away from LRM to NMT in 2001 required that the process be performed in accordance with FDA's QS regulations. NMT must demonstrate that its produced product, which adhered to the 510(k) cleared description of its product. The bottom line was that NMT's SNF could be better than the LRM's SNF, but it could not be worse. It must comply with the device described in the cleared 510(k)s.

106.



**D. Bard was experienced at selling SNF as a permanent IVC filter worldwide before it acquired NMT's IVC filter technology and began developing the RNF.**

107. Bard's sales force had been selling NMT's SNF devices in the United States and worldwide since the 1990's. Therefore, Bard before any clearance of the RNF already knew of the risks and rate of complications for the SNF, had the trained sales force available for aggressive marketing of IVC filters, and had established contacts with physicians implanting permanent IVC filters. Bard's QA/QC, engineers, and manufacturing had produced medical devices but did not have hands-on experience with NMT's design, development or manufacturer of IVC filters including either the SNF or RNF. NMT would continue to supply the SNF to Bard. Mr. Robert Carr, NMT's Senior Engineer would eventually transfer to Bard along with NMT filter technology and assume the role of RNF Project Team leader when Bard acquired the technology.

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<sup>91</sup>BPV-17-01-00058992

**E. NMT R&D developed and designed a “removable” IVC filter.**

**1. Initially Dr. Simon was involved with development of a “removable” IVC filter.**

108. NMT began development of a removable Nitinol filter in 1995. This would still be occurring under FDA’s GMP requirements without requirements for adequate design controls.

**a. Simon’s US Patent No. 5,669,933-1997.**

109. Dr. Simon’s removable Nitinol filter was submitted on July 17, 1996 titled “Removable Embolus Blood Clot Filter.” On September 23, 1997 it assigned US Patent No. 5,669,933. The other inventors listed were Stephen Kleshinski and Thomas Kinst. The assignee was “Nitinol Medical Technologies, Inc.” (NMT).

110. The initial Simon removable filter design proposed a collapsible Nitinol filter that could be collapsed toward a central axis to facilitate parenteral insertion into the IVC with imaging. There were two distinct groups of struts for the device (upper and lower) were present as in the SNF to help counterbalance the movement upward (cephalic) or downward (caudal) in the patient’s flowing blood stream. The upper arms (upper section) continued to prevent longitudinal movement of the filter in one direction in the vessel, with the lower legs preventing longitudinal movement in a “second direction opposite to the first direction. R. Simon had moved from the upper petal configuration to upward going curved arms and a lower conical cage to capture blood clots.”<sup>92</sup>

111. The next US Patent submitted by Dr. Simon on behalf of NMT was a ‘removable embolus blood clot filter’ was US Patent No. 5836968.

**b. Simon US Patent No. 5836968-1998**

112. According to the second Simon US Patent ‘Removable Embolus Blood Clot Filter’ assigned US Patent No. 5836968 on November 17, 1998, the upper filter arms, now hanging down lower were still intended to prevent movement of the filter longitudinally (in the vessel) in one direction, while the second lower group of legs were to provide a filter basket to catch the embolus and counterbalance the upper arms to prevent movement in a second direction opposite to the first direction. The conical cage was lost. The Simon design included an upper hook to aid the physician’s filter retrieval. The proposed device could be made of Nitinol, but Dr. Simon also proposed using other materials such as stainless steel and plastic.

**2. NMT proceeded without Dr. Simon to develop new removable IVC filter devices, and that work eventually became the basis of Bard’s “Recovery Nitinol Filter.”**

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<sup>92</sup> US Patent No. 5,669,933 Removable Embolus Blood Clot Filter. Inventors Morris Simon, Boston, MA, Stephen Kleshinski, Scimate, Thomas F. Kinst, Chelsea, MA. Filed July 17, 1996 and assigned September 23, 1997. Assignee Nitinol Medical technologies, Inc., Boston, MA

113.

[REDACTED]

[REDACTED]

[REDACTED]

114.

[REDACTED]

- a. **Ravenscroft US Patent 6,007,558: Prophylactic placement, elastic hooks, migration resistance for both a permanent and retrievable IVC filter, and no time recommendation for retrieval.**

115.

[REDACTED]

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<sup>93</sup> BPVE-01-00277852

<sup>94</sup> BPVE-01-00277852

<sup>95</sup> BPVE-01-00066044 at 66071

<sup>96</sup> Chanduszko deposition 10/13/2013, p. 92-93, L. 19-25.

<sup>97</sup> The '558 Patent.

[REDACTED]

116. [REDACTED]

117. NMT's US Patent 6,007,558 "Removable Embolus Blood Clot Filter" listed the inventors as Adrian Ravenscroft and Stephen Kleshinski, assignee NMT. In the "BACKGROUND," the application indicated the filter was intended to be removed after it had been implanted in the patient for a period of time.<sup>101</sup> There was no time recommendation for removal.

118. The patent described NMT's plans to market a new significantly modified IVC filter intended to be removed (retrieved) from a patient at some later date, still unspecified (several weeks or months) by a physician. The NMT US Patent was issued in December 1999 to NMT prior to Bard's formal acquisition of NMT's SNF/SL and Recovery IVC filter technology.<sup>102</sup> Bard was aware of the removable device development since it was funding the Dr. Asch study and NMT was planning to provide a demonstration device to Bard.

119. NMT's '558 Patent submission described a new indication for an IVC filter "prophylactic placement." Retrieval of the implanted filter from a patient was after an unspecified "period of several weeks or months." Features for a new capability to remove the filter were built into the product's new design. A temporary filter was viewed as able to help address patients' hesitancy and fears to receive permanently implanted filter devices, particular after the clotting risk had passed:

*patients are often averse to receiving a permanent implant, for the risk of a pulmonary embolism may disappear after a period of several weeks*

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<sup>98</sup> BPVE-01-00277852

<sup>99</sup> US Patent No. 5836968 Removable Embolus Blood Clot Filter. Filed July 16, 1997 and assigned November 7, 1998. Inventors: Morris Simon, Stephen Klesinski and Thomas Kinst, and assignee Nitinol Medical Technologies, Inc.

<sup>100</sup> BPVE-01-01351166

<sup>101</sup> Unlike the initial denied December 10, 1999, NMT 510(k) submission to FDA informing the FDA's reviewer that NMT was requesting only clearance to market its NMT Recovery Removable filter as substantially equivalent to the permanently implanted SNF (predicate), the new submission stated that the device was intended for the convenience of the physician for "intra-implant procedural" retrieval (to help a physician reposition a misplaced filter during insertion), a new use. BPV-17-01-00002677

<sup>102</sup> 2001 Bard acquired NMT "after more than one year of litigation." BPV-17-01-00051623

*or months. However, most existing filters are not easily or safely removable after they have remained in place for more than two weeks, and consequently longer term temporary filters which do not result in the likelihood of injury of the vessel wall upon removal are not available...*<sup>103</sup>

120. The Ravenscroft US Patent described the importance of the filters' design and functioning of the new 'elastic attachment hooks' in relation to stabilizing the device implanted in a patient and then permitting removal of the filter from the patient without creating trauma to the IVC wall. There was no discussion of 'intra-procedural' acute retrieval of the filter to reposition it during insertion as stated in NMT's 2000 denied 510(k) application. The US Patent described potential removal of an implanted filter after development of a layer of endothelium formed over the surface of the implanted filter (underlining added for emphasis).

#### **DETAILED DESCRIPTION**

*The structure of the hooks is important...these hooks are implanted and subsequently covered by the endothelium layer, they and the filter can be withdrawn without risk of injury or rupture to the vena cava.*

121. The Ravenscroft US Patent described the junction section (area) between the hook and leg. In contrast to the hooks of the SNF that had the role for stability, the proper elastic (give) functioning of this junction was considered critical to removal. The force (pull) placed on the filter at time of removal needed to be sufficient to straighten the hook out to permit its safe withdrawal.

122. The US Patent described the inventor's proposal that according to its pre-clinical laboratory testing model, with force applied in one longitudinal direction, a six-legged filter device provided a limit of 70 gms (0.145 lbs) of resistance force per leg when implanted in a 28mm test vessel. In the 28mm test vessel, the total load limit in terms of resistance to migration (holding the device stable as a permanent filter) was 420gm (0.93lbs)(< than one lb). Therefore, NMT assumed for a successful 'permanent' filter device, each leg hook should theoretically be required to be able to meet a release specification of 50mg pressure (force) to prevent device migration.<sup>104</sup>

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<sup>103</sup> '558 Patent.

<sup>104</sup> As not described in the '558 Patent application, the 28mm tube testing is static. It did not account for the motion and changes in pressure in the IVC of a living patient. Even in the *in vivo* sheep testing, the animal was not freely moving and engaged in its daily activities implanted with the filter when pressure values were obtained, which showed a 35mmHG pressure across the occluded filter. A better development model or more obvious choice should have been the SNF. It had been a successful IVC Filter when implanted in patients permanently, with good clot capture and stability. The primary challenge for NMT was stability as a permanent implant and retrievability.

123. NMT described the “elastic hook-leg junction” critical to the retrievable IVC Filter was made by grinding down (reducing the cross-section area) the leg wire and with “withdrawal force” would cause “flexure and straighten” releasing from the wall. There is no discussion about the difference in the withdrawal force by the physician and the forces placed on the filter in the IVC environment of a living patient which could also facilitate flexure and straightening of the hook to disengage from the wall (underlining added for emphasis):

*This junction section is considerably reduced in cross section relative to the cross section of the leg and the remainder of the hook. The junction section is sized such that it is of sufficient stiffness when the legs are expanded to permit the hook to penetrate the vena cava wall. However, when the hook is to be withdrawn from the vessel wall, withdrawal force to which the hook is subjected will cause flexure in the junction section so that the hook moves toward a position parallel to the axis of the leg...with the hook so straightened, it can be withdrawn without tearing the vessel....elasticity in the hook structure prevents the hook from tearing the vessel wall during withdrawal...*

*The load required to cause opening of the hooks can be modulated to the forces required to resist migration. This is accomplished by changing the cross-sectional area or geometry of the hooks, or by material selection.*

*...By reducing a portion or all of the cross sectional area of the hooks relative to that of the legs, stress is concentrated in the areas of reduced cross section when force is applied to remove the hooks from a vessel wall and the hooks become elastic and straighten....*

*This load is approximately 70 gms on each leg on a six-leg device for **50mm Hg.** pressure differential in a **28mm vessel.** The desired total load for the filter is desirably 420gms, and more legs with hooks can be added to lower the load for each leg...the object is to have the hook perform as an anchoring mechanism at a pre-determined load which is consistent with a maximum pressure of 50mm Hg.... It is the ability of the hook to straighten somewhat that allows the safe removal of the device from the vessel wall.<sup>105</sup>*

124. The US Patent further stated that the “elastic hooks” were to “ensure that the filter does not migrate in response to normal respiratory functions or in the event of a massive pulmonary embolism.”
125. The top’s retrieval hook used for Dr. Simon’s Removable Filter was modified by the Ravencroft US Patent to a loop. The upper group of arms pointed downwards and no longer provided a resistance (counterbalance) role. The upper arms were now called by the NMT inventors a basket to catch emboli and a mechanism to “center the hub at the trailing end of the filter within the vessel.” The lower group of legs also pointed downward and to which the hooks were attached,

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<sup>105</sup> ‘558 Patent.

no longer provided a counterbalance to resist motion and the upper arms, but were intended only to catch emboli.<sup>106</sup>

**b. Ravenscroft's Second US Patent No. 6,258,026B1 for a removable filter.**

126. NMT next submitted a new Ravenscroft patent application on July 26, 1999 for US Patent No. 6,258,026B1 titled "Removable Embolus Blood Clot Filter and Delivery Unit", assigned on July 10, 2001 to NMT. The inventors were listed as Adrian Ravenscroft and Stephen Kleshinski. There was no longer either a hook or a loop on the top of the filter to assist with retrieval.

**3. NMT RNF PowerPoint: "Critical Elastic Hook."**

127. [REDACTED]

128. [REDACTED]

129. [REDACTED]

130. [REDACTED]

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<sup>106</sup> *Id.*

<sup>107</sup> BPVE-01-00053098

[REDACTED]

131. [REDACTED]

132. [REDACTED]

133. [REDACTED]

134. [REDACTED]

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[REDACTED]

removed from nine animals. The goal of the experiment was “to prove that the RNF performed comparably to the SNF as a permanent filter.” The longest indwell time was six weeks.

#### **4. Ravenscroft US Patent for an Intravascular Snare**

135. The RNF Recovery System included another Ravenscroft patent but now ‘US Patent No. 6,458,145 B1’, submitted November 28, 2000 and assigned October 1, 2002. The inventors are Adrian Ravenscroft, Rochester, MA and Paul R. Gianneschi, of Snellville, GA. The assignee was not NMT, but rather ‘Hatch Medical LLC’, Snellville, GA. The device proposed was an intravascular snare constructed of Nitinol with gold or platinum iridium to provide opacity. The invention was a multi-looped intra-vascular snare of super-elastic Nitinol that was to provide improved wall coverage (greater wire to vessel surface area contact) and indicated it could be used for retrieval in a larger range of vessel diameters.<sup>113</sup>

#### **5. NMT Interacting with Bard to Fund Human Testing With its Prototype Removable Filter**

136. [REDACTED]
137. [REDACTED]
138. [REDACTED]

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and Anthony Venbrux, M.D., P. Rand Brown, DVM, Barbara Garibaldi, DVM, and Mark Evans, PhD (Pathology).

<sup>113</sup> US Patent No. 6,458,145 B1, Intravascular Snare and Method of Forming the Same” filed November 28, 2000 and assigned October 1, 2002. Inventors A. Ravenscroft and P. Gianneschi, assignee name hatch Medical LLC.

<sup>114</sup> BPVE-01-00242737

<sup>115</sup> BPVE-01-00277852

<sup>116</sup> BPVE-01-00277852

**F. The RNF did not perform “substantially equivalent” to the SNF when compared head-to-head for migration resistance.**

139.

[REDACTED]

[REDACTED]

140.

[REDACTED]

141.

[REDACTED]

[REDACTED]

---

[REDACTED]

[REDACTED]

121

142.

[REDACTED]

[REDACTED]

**1. RNF Filters failed to show adequate migration resistance compared to SNF before Bard submitted an RNF 510(k).**

143. [REDACTED]

144. [REDACTED]

145. [REDACTED]

146. [REDACTED]

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<sup>124</sup> BPV-17-01-00002650

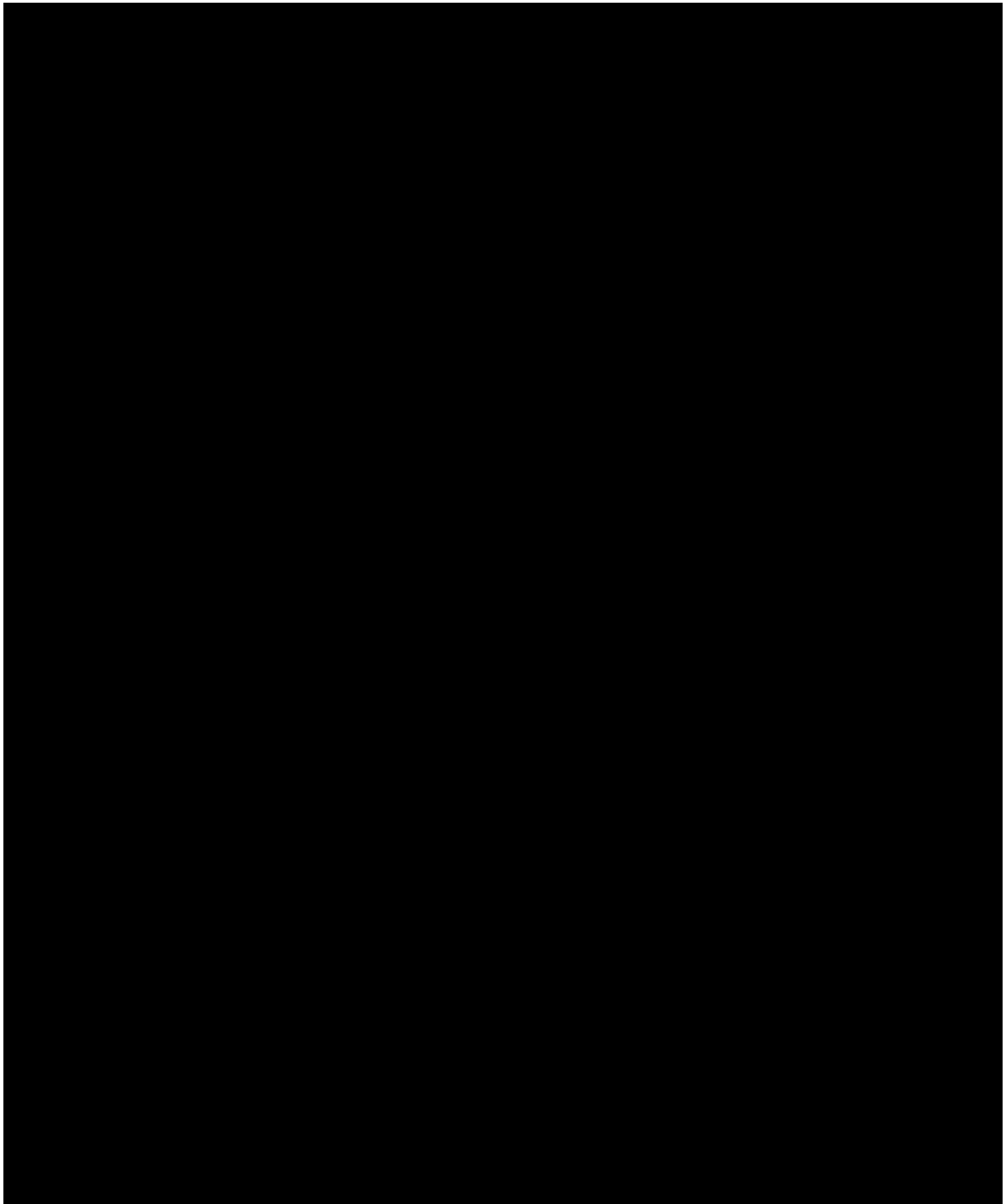
<sup>125</sup> BPV-17-01-00072740

<sup>126</sup> BPV-17-01-00072740.

<sup>127</sup> BPV-17-01-00072746

<sup>128</sup> BPV-10-00002650.

<sup>129</sup> BPVE-01-00410985



148.

149.

150.

151.

152.

[REDACTED]

153. [REDACTED]

154. [REDACTED]

155. [REDACTED]

156. [REDACTED]

[REDACTED]

[REDACTED]

157.

[REDACTED]

158.

[REDACTED]

[REDACTED]

159.

[REDACTED]

160.

[REDACTED]

[REDACTED]

[REDACTED]

161. [REDACTED]

162. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

163. [REDACTED]

[REDACTED]

164. [REDACTED]

[REDACTED]

Dr. Robinson stated “Literature states about 70mgHG is generated in completely occluded cava.”<sup>151</sup>

165. In 2014, the medical literature shows that taking into account patient breathing and Valsalva, the mean pressures of the IVC are in the 74-81mm Hg range.<sup>152</sup>

**H. Bard acquired all of NMT’s RNF technology in 2001.**

166. [REDACTED]

**1. In 2001, when NMT transferred SNF’s production in-house, an SNF specification was created which included migration resistance and leg span.**

167. [REDACTED]

168. [REDACTED]

169. [REDACTED]

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<sup>151</sup> BPV-17-01-00045882

<sup>152</sup> Laborda A, et al. Influence of breathing movements and Valsalva maneuver in vena cava dynamics. World J Radiol 2014 Oct 28; 6(10):833-9

<sup>153</sup> BPVE-01-00242737, NMT’s last FDA cleared 510(k) was the SNF in April 1997 (K970099)

<sup>154</sup> BPV-17-01-00058992

[REDACTED]

170. [REDACTED]

171. [REDACTED]

172. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

173. [REDACTED]

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<sup>155</sup> SA-0047.00 Filter, NMT Annealing Jig Qualification Data, RD-RPT-136 SNF Hook Sharpening Verification Report

<sup>156</sup> BPV-17-01-00058992

<sup>157</sup> BPV-17-01-00058992

[REDACTED]

174. [REDACTED]<sup>158</sup>

[REDACTED]

175. [REDACTED]

176. [REDACTED]

177. [REDACTED]

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<sup>158</sup> BPV-17-01-00058992

<sup>159</sup> BPVE-01-00242737

<sup>160</sup> BPVE-01-00242737

<sup>161</sup> BPVE-01-00242737

<sup>162</sup> BPVFILTER-01-00003802

internationally in 2002 and in the USA in 2003. The new RNF product would be key to helping Bard drive both IVCF market expansion and share growth in the area.

**3. Acquisition of the new RNF System was intended to expand Bard's IVCF market and increase market share.**

178. Bard knew that as of July 2001 the RNF had been successfully able to be implanted and removed in animals and in approximately 30 human patients (see Dr. Asch's study in Canada).<sup>163</sup>

[REDACTED]

179. [REDACTED]

180. [REDACTED]

[REDACTED]

The sponsor of the IDE would also propose the success and failure endpoints.<sup>165</sup> The IDE also requires the sponsor to list the clinical trial and outcome information with the National Institutes of Health clinical trials database (<http://www.clinicaltrials.gov>).

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<sup>163</sup> Asch MR. Initial experience in humans with a new retrievable inferior vena cava filter. *Radiology* 2002 Dec. 2002; 225(3):835-44 (DOI:10.1148/radiol.2252011825)

<sup>164</sup> BPVE-01-00242737

<sup>165</sup> The FDA's IDE process is described in 21 CFR § 812.

**4. Bard's sales force was already trained and waiting to aggressively sell IVC filters to physicians in the United States.**

181. In July 2001, Bard's Peripheral Technologies (BPT) had 43 representatives already in the USA available to sell both the SNF and RNF. This sales team had sold IVC filters (SNF) since 1992 in the USA and possessed the expertise and physician relationships necessary to successfully sell Bard's IVC Filters to both radiologists and vascular surgeons. Therefore, in 2001 Bard saw the sales force as already assembled, trained and in well-situated in the USA to be able to sell both the SNF and RNF to physicians. The Bard sales force just needed to receive a new and improved IVC filter like RNF to sell.

**5. Bard should have been aware RNF had significant new safety issues not seen with SNF by results of Dr. Asch's small short-term retrieval study.<sup>166</sup>**

**a. Bard funded Dr. Asch's clinical retrieval feasibility study.**

182. Murray Asch, MD was the clinical trial director of a clinical trial conducted in Toronto Canada at Mt. Sinai Hospital to examine retrieval of the RNF. He testified that originally Bard was going to include a United States physician, but then he was told in May 18, 1999 that letter from Ms. M. Coutanache, Bard Canada's Director of Marketing and T. Kinst, NMT that the "regulatory burden for using the filter on a compassionate grounds" was too great a burden to use a physician from the United States.<sup>167</sup> He was told that the device manufactured by NMT could stay in patients 6 months.<sup>168</sup> He testified that he also would have done a long-term implant study at that time if asked to by Bard.<sup>169</sup> If he had been told the study was to be used for the FDA he would have designed the study "in a different way." The plan communicated to him by Bard was that he was "going to do a pilot study to help open the doors for a large multi-center American study, which would be utilized to obtain FDA approval."<sup>170</sup> Bard described this study to him as an "initial feasibility study, safety study, let's get the ball rolling, let's see if this device will perform in humans as it has in animals and in the lab. And then once we know it is safe, it will be easier to obtain approval for a real-a bigger study in the United States."<sup>171</sup>

*Q. Does a doctor working with a medical device company expect the company to be honest and transparent in working with you?*

*A. I absolutely expect that.*

*Q. Do you expect the company sponsoring the study to put patient safety first?*

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<sup>166</sup> Asch deposition 5/2/16, p 109-111; L.23-8.

<sup>167</sup> Asch deposition 5/ 2/16, p.15-16, L.6 -6, Asch Exhibit 202

<sup>168</sup> Asch deposition 5/2/ 16, p. 18, L. 7-17

<sup>169</sup> Asch deposition 5/2/16, p. 20, 12-17

<sup>170</sup> Asch deposition 5/2/16/p. 23, L. 7-24

<sup>171</sup> Asch deposition 5/ 2/16, p. 24-5, L. 6-2

*A. Yes I do.*<sup>172</sup>

183. The Asch trial was started on April 25, 2000. For twenty-one (21) patients the RNF remained implanted 26 days or more of a population of thirty-five (35) RNF patients. The retrieval patients were implanted with a filter (26-134 days), the average was 58 days. There were 22 (63%) insertion/deployment procedural difficulties, 5 reports of tilt (14.3%,  $\geq 20$  degrees), 1 migration and 1 fracture (3%). According to the report of the Dr. Asch retrieval trial, an investigation to the procedural difficulties (insertion & deployment) determined that the filter spline was being over-polished during manufacture, which was thought to cause the difficulties and partial device openings. As a result, the polishing process was modified after Patient #23. No further incidences of difficulty release or partial device opening were reported after the modification.<sup>173</sup>

**b. Dr. Asch's short-term retrieval study in patients demonstrated RNF risks for tilt, migration, perforation and fracture.**

184. Looking at a one page summary table like intended for perhaps a poster presentation titled "Clinical Trial" the data was for 35 implanted patients, with 27 filters (77.1%) reported as retrieved, 5 (14.3%) patients with filters not yet removed and 3 (8.6%) patient deaths. Of the 27 patients with filters removed, 3 (11%) had 1-2 legs incorporated into the caval wall; 1 (4%) had transmural incorporation, 1 (4%) had a filter leg seen outside the vessel lumen, 1 (4%) had questionable caval narrowing at the filter site, 1 (4%) with mild caval stenosis, 1 (4%) with increased tilt from the baseline with slight penetration of the wall, 1 (4%) migration of 4 cm<sup>174</sup>, 1 (4%) filter arm fracture with missing leg hook, and 17 (63%) cases with no change in filter placement or disruption of caval wall.

185. With the first case of a filter migration, Dr. Asch testified he "essentially stated the study would be stopped until there was an investigation. It was relatively early in the study so—the relative incidence of a potentially serious complication was high, and I was concerned about proceeding again with a previously-untested human device. This was in Bard's hands, so Bard did a root-cause analysis"<sup>175</sup> He did not recall if he received a copy of the investigation, but he did not recall they determined the problem or changed manufacturing.<sup>176</sup>

*Q. Did you make the decision to go forward with the study after receiving Bard or NMT's root-cause analysis in discussing their evaluation?*

*A. Yes. We had extensive discussions at that time and felt, based on the close monitoring of patients, that it would be reasonable to proceed*

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<sup>172</sup> Asch deposition 5/ 2/16, p. 24, L. 20-23

<sup>173</sup> Fuller Exhibit 120

<sup>174</sup> BPV-17-01-00057953

<sup>175</sup> Asch deposition 5/ 2/ 16, p. 29-30, L. 24-14

<sup>176</sup> Asch deposition 5/ 2/ 16, p. 30-31, L. 24-13

*with the understanding that if another complication-another serious complication occurred, we would terminate the study.*<sup>177</sup>

**c. NMT/Bard's Failure Investigation for Filter Migration**

186. A September 1, 2000 R&D Technical Report, Document RD-RPT-128 titled "Investigation Report of a Migrated Recovery Filter in Human Use Experience at [redacted]" was issued by Mr. Carr. At that time the longest patient implanted (134 days) had shown the RNF implanted device on imaging with filter arms outside of the IVC (perforated) following abdominal surgery. At time of this caval perforation report only 11 filters were implanted and five were removed by Dr. Asch.

187. [REDACTED]

188. [REDACTED]

189. [REDACTED]

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<sup>177</sup> Asch deposition 5/ 2/ 16, p. 31-32, L19 -3

<sup>178</sup> Carr Exhibit 7

<sup>179</sup> Carr Exhibit 7

<sup>180</sup> Carr Exhibit 7

<sup>181</sup> Carr Exhibit 7

<sup>182</sup> Carr Exhibit 7

<sup>183</sup> Carr Exhibit 7

190.



**d. RNF showed 10% migration rate with “increased careful monitoring of filter status” in Dr. Asch’s patients.**

191. Thomas Kinst of NMT wrote a September 14, 2000, memo that said, “During the discussion, the following questions were asked by the Bard group: Given the compassionate use data to date, it can be stated that the Recovery Filter has a 10% migration rate.”<sup>189</sup> The memo continued, “Only large controlled clinical study can definitively assess it.”<sup>190</sup> The plan for the Dr. Asch study was to obtain abdominal scans or x-rays ever two weeks to assess the location of the filter. The study became a very closely followed study.

*Q. Does that happen to regular filter patients in the real world?*

*A. That does not happen in every day practice, that is right.*<sup>191</sup>

**e. Dr. Asch described patient #33 with fractured arm, hook, tilt, and perforation which significantly differed from Bard’s descriptions in its FIR and information provided to FDA.**

192. Patient #33 in the Asch study a 29-year old woman near the end of her third trimester of pregnancy. Dr. Asch described the CT scan of April 2, 2002, and noted a malposition of the filter arm as well as a suspicion of caval perforation of the leg. The patient’s filter subsequently was found to have tilted approximately 15 degrees from baseline, a fractured filter arm fragment was seen in imaging adjacent to the right renal vein, there was a possible perforation of the leg outside the IVC on imaging. At time of retrieval the fractured filter hook could not be found but which was thought to have been “presumably” located at the site of caval perforation. The clinical event report for RNF in a pregnant woman also did not correspond to the later Cheung (2005) published study comparing the success of the RNF retrieval in a pregnant woman at longer indwell time, misstating the performance of the RNF when compared to the retrievable Tulip filter available in Canada for retrieval and used in a pregnant woman. The authors recommended RNF for a new patient population, namely pregnant women to temporarily prevent PE, but failed

<sup>184</sup> BPV-17-01-00067972; BPV-17-01-00072740

<sup>185</sup> BPV-17-01-00067972

<sup>186</sup> BPV-17-01-00067972

<sup>187</sup> BPV-17-01-00034448

<sup>188</sup> BPV-17-01-00034448

<sup>189</sup> Asch Exhibit 203

<sup>190</sup> Asch Exhibit 203

<sup>191</sup> Asch deposition 5 16 p. 35-36, L 22-1

to describe the problems with the RNF in patient #33.<sup>192</sup> Dr. Asch wrote that for Patient 33 with a “fractured filter” he contacted both Bard (distributor) and NMT (manufacturer). Dr. Asch testified that his discussions for the study were with Robert Carr as an engineer for NMT<sup>193</sup> but he did contact Bard about Patient #33:

*I did contact the filter distributor and manufacturer to inform them of the filter fracture today. I will make arrangements for the filter to be shipped back to the manufacturer for evaluation. HPB, and the Hospital Ethics Board were informed of this condition.*<sup>194</sup>

193.Dr. Asch testified that this woman’s filter had two fractures.

*Q. What happened to patient 33?*

*As a result of the close monitoring of these patients, we were able to identify the fractures and we were able, fortunately, to safely retrieve the filter before a more serious adverse event could have occurred.*<sup>195</sup>

...

*Q. And about how long was that piece of metal?*

*A. About one inch.*

*Q. And is a one-inch piece of metal in your vena cava something that would concern you as far as the patient’s safety?*

*A. Yes, because that piece of metal could have then migrated either to the heart or lungs where it could have been lethal.*

*Q. So a fracture is potentially a danger—a deadly complication?*

*A. Yes*

*Q. Can patients die from fractures?*

*A, Yes, patients can die.*

*Q. Did you stop the study again---*

*A. Yes*

*Q---for patient safety*

*A. Yes*<sup>196</sup>

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<sup>192</sup> Cheung MC, Asch MR, Gandhi S, Kingdom JCP. Temporary inferior vena caval filter use in pregnancy. *J Thromb Haemost* 2005; 3:1096-7; Asch (2002)

<sup>193</sup> Asch deposition 5/2/16 p. 40, L. 11-18

<sup>194</sup> Fuller Exhibit 121

<sup>195</sup> Asch deposition 5/2/16 16 p. 36, L. 16-21

<sup>196</sup> Asch deposition 5/2/16 p.37, L. 1-22

*Q....but you had the second break where the anchor, the foot broke off as well; is that right?*

*A. That's correct.*

*Q. Were you able to find that in the patient?*

*A. We were not.*<sup>197</sup>

*Q. Did the problem of the fractures in Patient 33 concern you?*

*A. Very much*

*Q. Why is that?*

*A. Although I had previously placed many fractures—many filters, I personally had never seen a filter fracture before and, again, being aware of the potential lethal complications of a filter fracture, particularly in a brand new device that had not been tested over long term or widely, it was very concerning.*

*Q. And did you express those concerns to Bard?*

*A. Yes*<sup>198</sup>

194. What Dr. Asch says he was told about the filter for Patient #33 was that there was potential weakness at the site of the weld and there was potential for increasing the “robustness” of the device by manufacturing it with a larger diameter wire.<sup>199</sup> He believed that Rob Carr told him that Bard was going to change the design or manufacturing process to try to prevent filter fractures. He expected Bard to have done a proper root-cause analysis to identify the cause of the fractures and to make the changes to prevent filter fractures in the devices they would make. They had already made changes to the spline problem, so he assumed that Bard would make changes for this problem as well.<sup>200</sup> After discussion with Rob Carr and others at Bard, Dr. Asch continued the study because patients were monitoring so closely and he had the expectation that a new filter design would be coming out shortly.<sup>201</sup>

195. The event occurred in April 2002, and the Dr. Asch study for publication as a Phase 1 study was already submitted for the first 32 patients. Patient 33 was not included in the published study.<sup>202</sup> He was not informed that Bard was applying to the FDA for marketing clearance at the time of the submitted publication.

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<sup>197</sup> Asch deposition 5/2/16 p. 38-39, L18-1

<sup>198</sup> Asch deposition 5/2/16 p.38-39, L. 12-1

<sup>199</sup> Asch deposition 5/2/16 p.40-41, L. 19-2

<sup>200</sup> Asch deposition 5/2/16 p.41, L. 4-21

<sup>201</sup> Asch deposition 5/2/16 p. 42, L. 12-19

<sup>202</sup> Asch deposition 5/2/16 p.38, L. 7-17

**f. Bard's FIR for Patient #33's Filter Fractures Was Flawed and Minimized Risk**

196.

[REDACTED]

197.

[REDACTED]

198.

[REDACTED]

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<sup>203</sup> Fuller Exhibit 122

<sup>204</sup> Fuller Exhibit 122

[REDACTED]

199. [REDACTED]

200. [REDACTED]

201. Dr. Asch said he learned that the FDA cleared the RNF for marketing sometime after the submission of the manuscript<sup>206</sup>, probably around Jun 2002. He recalled that someone, probably Monica, the sales force person in contact with him regarding sales issues had told him. He had assumed that his study was only a pilot study to look at feasibility of “retrievability” not as a long-term filter safety study. He indicated he thought that there would be a future larger “real” safety study as well as changes made to the final device for manufacturing.

*Q. Did you have any discussions with Rob Carr, Monica, or anyone else at Bard about the advisability of taking the filters to market at that time.*

*A. Yes, all along I had been consistent in my beliefs and concerns that this was a pilot study to assess simply retrievability. This was not a long-term safety study with respect to the filter and it had been always my expectation that this was going to be a pilot study to lead into the study that would truly assess or not this was a safe and effective filter.*

..

*Q. Did you ever tell them that it wasn't ready to be released to the public?*

*A. Yes. Again, I told them that this should not be released until a real study was done.*

*Q. And why was that?*

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<sup>205</sup> Fuller Exhibit 122

<sup>206</sup> Asch Exhibit 209; Asch (2002)

*A. Because, although we had assessed safety and feasibility of retrievability, the title of the study, we had never assessed for the safety of leaving the filter in place.*

...

*Q. What was your concern, Doctor?*

*A. My concern was that there was no scientific evidence that this brand new device was tested and safe and ready to be released into the general public for widespread use.*

*Q. And what was Bard's response to you when you raised safety concerns?*

*A. Their response was, we plan on doing a large multi-center prospective American study to assess those questions.*

*Q. So you felt they addressed your concern when you told them that the filter needed more studies?*

*A. Yes, I felt that.*

*Q. And who made you that promise?*

*A. Pretty much everyone. Again mostly, I felt it was mostly Monica as a Bard representative and the American Bard people who were most responsible for ensuring that that was going to happen.<sup>207</sup>*

...

*Q. So the study they told you was going to occur did not occur?*

*A. That's correct.*

*Q. And how did that make you feel, Doctor?*

*A. It made me feel deceived and betrayed. They made me a promise. I felt responsible because, as a result of the work that I did under certain conditions, they took that data to get the device approved, and subsequently released into the general market without appropriate safety testing.<sup>208</sup>*

202. Ms. Fuller testified that she was told that the filter fractured because the woman was in her third trimester of pregnancy.<sup>209</sup> Ms. Fuller also testified that she had asked for further information on the fractured hook as to root cause.<sup>210</sup>

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<sup>207</sup> Asch deposition 5/2/16, p. 43- 45, L.22 -17

<sup>208</sup> Asch deposition 5/2/16, p. 46, L. 8-22

<sup>209</sup> Fuller Exhibit 122

<sup>210</sup> Fuller Deposition 2016, p 93-97 L5-2

*Q. Was there ever an instruction of warning about the use of this product in pregnant women?*

*A. I—I'm not sure.* <sup>211</sup>

**g. Bard's Senior Regulatory Specialist Reportedly Had Concerns About RNF Safety and Adequacy of Bard's Failure Investigation**

203. Bard was aware of the Patient #33 failure of the Recovery filter as of April 2002. On June 21, 2002, Carol Vierling, an individual located at Bard in Covington, GA responsible for SNF filters and a member of the RNF team<sup>212</sup> forwarded the draft failure investigation report for the RNF and Pt. #33 on to Kay Fuller.<sup>213</sup> Ms. Fuller had only joined Bard as a Regulatory Specialist in March 2002 and had been assigned to the RNF Team. Instead of the information in the original May 2002 investigation and the final July 9 2002 report about for Patient 33, this June draft version had that “*during the removal procedure, the small hook fractured and **remained in this tissue**, although it is not visible with available equipment.*” Ms. Fuller upon viewing the report had written next to the statement “*Is this true/accurate?*”<sup>214</sup> She was later asked to explain the significance of the written note:

*Q. So what was your response to the corrective action and to—to the results of the investigative report?*

*A. Well, I—I had several concerns about the—this failure investigation report, first and foremost, the report—the first reports I saw had not been fully signed off. ...*

*I was concerned that, you know, the report, the first report I saw had been conducted, I believe in 2001. Because again, this failure occurred in Patient 33, in Dr. Ash's study in Canada. Once that happened, they're required to retrieve that device and send it to the company, so that they could do the failure investigation. And typically, that's done very, you know, rapidly.*

*So here it was months and months later, where I was finally seeing the failure investigation...*

*But once I started looking at the report further, ...I really became concerned that they did not get to the real root cause of these fractures.*

*Q. Why...*

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<sup>212</sup> Fuller deposition 1/11/16, p 260, L. 12-2

<sup>213</sup> Fuller Exhibit 123

<sup>214</sup> Fuller deposition 2016, p 100-104 L 6-17

*A. Well, because, in order to make sure the device is safe and effective, we need to understand why a device would fracture in a small clinical study, especially with the rate of fracture being more than 3 % in that study. And the better we understood the root cause of why the metal broke, then the better chance we would have of putting in an adequate and effective corrective action to assure that any future device would not fracture.*

*Q. And were you the person who would have to explain this to the FDA or to put it in the language that the FDA would understand?*

*A. Typically...we were going to typically address this in the 510(k) application...as a regulatory person, you're always trying to anticipate what are the key safety features that the FDA is going to focus on for a product.*

*...this certainly would cause question for the FDA....*

*Q. What was your personnel concern about a 1 in 35 fracture in the clinical study?*

*A I was certainly concerned that the product broke in such a small study. And the reason I was so concerned is devices are not supposed to break once they're implanted in a patient. Rule number 1, device needs to perform as intended. If a device breaks after it's implanted, then it's not performing as intended, and its unsafe....*

*...*

*...If we didn't drive to understand the root cause of the failure, why the metal fractured, if we didn't understand as a team from an engineering standpoint and even maybe the clinical standpoint, then how could we assure that the future Recovery Filters would not break?...I was concerned that this could lead to additional patient injury, and potentially death.*

*...There's a basic rule of thumb in the device industry that failure modes that could lead to serious injury or death should certainly not be happening more than a 1%, and it should stay well under a 1%, failure rate....*

204. Ms. Fuller said that seeing the June draft report for Patient 33 as a regulatory person raised a red flag to her.<sup>215</sup> She continued that once she started looking at the report further, she really "became concerned that they did not get to the real root cause of these fractures."<sup>216</sup>

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<sup>215</sup> Fuller deposition 1/11/16, p. 101, L.2

<sup>216</sup> Fuller deposition 1/11/16, p. 101, L.6-9. The SNF by a NMT 1997 Technical report had a fracture rate of .006 referencing a report by McCowan (1992).

**h. Bard's regulatory specialist questioned Bard's FIR conclusion the filter showed "ductile" failure.**

205. The May 6, 2002, failure investigation contained photographs of Patient 33's fracture site which was called "ductile" change in the metal. Ms. Fuller took the information and photographs to an engineer she had worked with a Bard on another project, Ann Bynon. Ann told her that the changes were not ductile as called in the NMT report but classic of a "*brittle*" fracture. Ms. Fuller was concerned that the information about "*ductile*" was incorrect. She knew that a report intended for FDA needed to be correct.<sup>217</sup> She went to another engineer, Alex, and he would not discuss the fractures with her and following that encounter "I believe there was some repercussions to those discussions."<sup>218</sup> Her supervisor Mary Edwards asked her why she was shopping around for failure investigation to engineers outside the Recovery Team Core to get opinions. Ms. Fuller provided the context of the discussion she had with Mary Edwards:

*A. Her concerns...had to do with she was getting pushback from one of the team members on the Recovery team—core team. That the leader of that Recovery team development team was her that I needed to quit doing that. And if I didn't quit getting advice from other engineers, that I would basically be not allowed to stay on the team. That Rob Carr<sup>219</sup> didn't want me to be on the team if I kept doing this, that I wasn't being a team player. Basically, words that really stunned me coming from my boss, the regulatory vice president of the company.*

*And I remember saying to the effect "Are you kidding me, Mary?" This is exactly what we're supposed to be doing."<sup>220</sup>*

206. Ms. Fuller requested and eventually got to see the 10-year cycling simulated use of the filter. When she read the report, she said "she was concerned since FDA for a 510(k) usually requires what device you tested, what lot, what batch, and under what conditions. When she read the report, she reportedly realized they didn't state in the report that this 10 year- simulated use test utilized post-sterilized device samples, she was very concerned about that."<sup>221</sup>

**i. Bard's regulatory specialist reportedly refused to sign RNF's 510(k) cover letter, Truthful and Accuracy Statement, and Bard's RNF Fact Book.**

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<sup>217</sup> Fuller deposition 1/11/16, p. 110-111, L. 14-

<sup>218</sup> Fuller deposition 1/11/16, p. 113, L. 5-15

<sup>219</sup> Robert Carr according to Ms. Fuller came from NMT, she thought he was an engineer at NMT for the RNF and SNF. He was the head engineer, Project Leader with the long history of the product. Fuller deposition p. 115

<sup>220</sup> Fuller deposition 1/11/16, p.114-115, L. 24-20

<sup>221</sup> Fuller deposition 1/11/16, p 115- 117, L. 17-

207. Ms. Fuller testified that when she looked at the small clinical study conducted in Canada with RNF (the Dr. Asch study) she noted that there were some complications.<sup>222</sup> She stated that what really stood out to her in the 35-patient study was “oh my goodness, we had a fracture really jumped out at me.”<sup>223</sup> She continued that “there had been some challenges with the device titling, once implanted, one example of the filter actually migrating, which any three of those could lead to serious injury or death, under certain scenarios.”<sup>224</sup>

*Q. Tell me why you were concerned about the fracture.*

*A. Well, the fracture is a ---potentially catastrophic failure. If you have a fracture, the component fractures off, the piece that fractures off, can migrate and can be considered a dangerous embolism...It can be dislodged into other parts of the body. It could also end up landing in the heart, for example.*

*...that's a failure you never want to see in any medical device, and I was especially concerned because they only had 35 patients, so it would have been in this small setting of more than 3%, and that would be alarming.*<sup>225</sup>

208. Ms. Fuller said that normally there is one signature and it would have been her signature. However, she did not sign the cover letter, but it was signed by Carol Vierling.<sup>226</sup> She also testified that she never authorized anyone to sign the cover letter for her. She was asked:

*Q. ...And did you sign this letter accompanying the submission?*

*A. No, I did not.*

*Q. Why not?*

*A. I was concerned about the things we've been discussing.*

*Q. Specifically.*

*A. Specifically, that I didn't feel like we adequately addressed the fracture failure mode, and put in an adequate corrective action. And I was most concerned also that the 10-year simulated cycle testing had been conducted on a pre-sterilized device. I was most concerned that this product might have problems and might have some failure modes that could hurt people.*

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<sup>222</sup> Fuller Exhibit 120.

<sup>223</sup> Fuller deposition 1/11/16, p. 86, L. 6-11

<sup>224</sup> Fuller deposition 1/11/16, p. 86, L. 6-19

<sup>225</sup> Fuller deposition 1/11/16. P. 87, L. 7-21

<sup>226</sup> Fuller deposition 1/11/16

*Q. ...Did you ever authorize anyone else to sign this document in your behalf?*

*A. No, I did not.*<sup>227</sup>

209. Kay Fuller was listed on the CDRH Submission form dated July 8, 2002 for the Special 510(k) as the Bard contact person.<sup>228</sup> She was asked about the Truthful and Accuracy Statement in the 510(k).

*Q. ...Did you sign this?*

*A. No, I did not.*

*Q. Who did sign it?*

*A. Carol Vierling.*

*Q. And why did you not sign it?*

*A. Because I take the signing of the Truthful and Accuracy Statement very seriously. It's my responsibility to make sure that everything we're submitting to the Agency is truthful and accurate, and that we haven't omitted pertinent facts. And I was uncomfortable signing that. It's really the first time and only time in my career I was not comfortable signing that in an application to the FDA.*

210. Bard's Declaration of Conformity with Design Controls for the Special 510(k) was signed by Lynne Buchanan-Kopp, the Senior Quality Assurance Engineer at the Tempe site. A second version of the same document was signed by Pete Palermo at the Glen Falls site.<sup>229</sup> Ms. Fuller was asked about the signatures for the 510(k) submission:

*Q. And therefore, Carol Vierling, Lynne Buchanan-Kopp, and Pete Palermo all signed Truthful and Accuracy statements or Declarations of Conformity that accompanied the 510(k) application. Correct?*

*A. That's correct.*<sup>230</sup>

**VIII. BASES FOR OPINION #2: BARD OBTAINED FDA CLEARANCE TO MARKET THE RNF AS BOTH A PERMANENT & RETRIEVABLE IVC FILTER YET FAILED TO PROVIDE PHYSICIANS AND PATIENTS WITH ADEQUATE, UPDATED "INSTRUCTIONS FOR USE" AND "WARNINGS OF RISKS."**

Bard, not the FDA, is responsible for ensuring the adequacy of its labeling and marketing. To obtain clearance for the RNF from the FDA, Bard claimed it was

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<sup>227</sup> Fuller deposition 1/11/16, p129- 130, L. 22 -15

<sup>228</sup> Fuller Exhibit 127

<sup>229</sup> Fuller Exhibit 136

<sup>230</sup> Fuller deposition 1/11/16, p. 279, L. 12-16

substantially equivalent to the permanent SNF, despite not having data to support safe and effective permanent use. Bard's labeling and marketing failed to adequately instruct (IFU) and warn implanting physicians, physicians caring for permanently implanted patients (e.g., surgeons, hematologists, internists, emergency medicine), and patients about the potential post-market risks, including the need for the patient to continue to be monitored for filter complications and the need for appropriate placement (stability) when permanently implanted. When Bard had the RNF cleared for the "option" to be used as a temporary IVC device, Bard continued to fail to adequately and voluntarily update its labeling, IFU, and warnings to include recommendations for indwell time range and warnings describing updated post-market risks. Bard, not the FDA, was required to provide implanting physicians, retrieving physicians, and physicians caring for implanted patients with an updated labeling describing risks of tilt, migration, fracture, embolization; difficulties with retrieval perforation; the potential for revision surgery; and the need to plan for removal of the RNF filter when no longer clinically indicated.

**Applicable Regulations:** 21 CFR § 807; 21 CFR § 801.109; 21 USC § 331(a)(b); 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n)

**A. Bard Cleared the RNF by claiming the RNF was as safe and effective as the permanent SNF IVC filter.**

211. Kay Fuller, RAC, is a certified regulatory affairs specialist. She joined Bard on March 25, 2002, and was Bard's Senior Regulatory Affairs Specialist for the initial RNF 510(k), resigning on April 1, 2003 before Bard received the 510(k) clearance of a RNF retrieval option. She was the designated regulatory member of Bard's RNF development team and developed the successful two-tier (permanent then retrieval option) strategy, which resulted in the December 2002 clearance of the RNF for retrieval. She also was the lead person for the preparation of the initial Special RNF 510(k) (K022236), its submission and all interactions and responses with the FDA.<sup>231</sup> She stayed on the RNF project until her resignation from Bard February 2003 when working on the drafting of the retrieval option Abbreviated 510(k). When she was initially assigned her job with RNF, she "didn't know much" about the Recovery Filter.<sup>232</sup> She would testify that learning about the RNF history she identified that NMT had actually designed and developed the prototype device and that NMT had submitted a 510(k) for the RNF and had received NSE letters denying clearance.<sup>233</sup> She thought that there had been two NMT 510(k)s denied, one filed by Sherry Goldsmith of NMT and then another by attorney Howard Holstein prepared by Hogan & Hartson.<sup>234</sup>

<sup>231</sup> Fuller deposition 1/11/16, p. 61- 62, 20-5

<sup>232</sup> Fuller deposition 1/11/16, p. 62, L10-17

<sup>233</sup> Fuller deposition 1/11/16, p. 62-63, L. 20-13

<sup>234</sup> Fuller deposition 1/11/16, p. 64, L. 3-18

<sup>235</sup> Fuller deposition 1/11/16, p. 65, L. 3-13

212. She was asked about her obligations in 2016 with the RNF for Bard and if the RNF clearance, when she was involved with the submission, was viewed as a high priority project to be accomplished when she was at Bard:

*Q. ---so this spells out your obligation, your duty and responsibility to the FDA?*

*A. Yes*

*Q. Now, the FDA is- operates on an honor system, doesn't it?*

*A. In a sense, yes.<sup>236</sup>*

*...*

*Q. ...did the FDA do any testing on their own?*

*A. Not to my knowledge.<sup>237</sup>*

*Q. Was there a retrievable device on the market that had already been approved in the United States at that time?*

*A. Not that I---I recall.*

*Q. Where did Bard rank this in importance, if the told you...*

*A. It became pretty clear early on, after I joined the company, that this was a very exciting product. That it was going to be potentially the first vena cava filter that could be actually permanently implanted and retrievable. And so, partly because of the history of how many years they had spent trying to get FDA clearance on the Recovery Filter, it had been moved to the top of the divisional company goals. So the Temp facility, it was the number 1 project goal for Bard Peripheral Vascular in Tempe.*

*Q. So did your job duties include designing a regulatory strategy to try to get clearance for the Recovery device?*

*A. Yes, it was one of my key assignments early on, again, they had received these two non-substantial equivalent letters earlier in the history of the development of this device. So, we understood that there was possible that the FDA would require us to conduct a full on-clinical study. And one of the things I was asked to --is there a way we could get this Recovery Filter through the FDA clearance process without having to conduct a very large, expensive clinical study.*

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<sup>236</sup> Fuller deposition 1/11/16, p. 47, L. 5-10

<sup>237</sup> Fuller deposition 1/11/16, p. 47, L. 18-21

*And so, I started looking for opportunities to be able to creatively create a strategy that would help reduce the likelihood that we would need to do a clinical study.*

*Q. And were you able to design such a strategy?*

*A. Yes, I was.* <sup>238</sup>

213.

[REDACTED]

214.

[REDACTED]

215.

[REDACTED]

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<sup>238</sup> Fuller deposition 1/11/16, p. 65-67, L. 21-8

<sup>239</sup> Fuller deposition 1/11/16, p. 68-72 L. 5-13.

<sup>240</sup> Fuller deposition 1/11/16, p. 73, L. 1-18

<sup>241</sup> BPV-17-01-00051623

<sup>242</sup> Fuller deposition 1/11/16, p 260, L. 12-2

<sup>243</sup> Fuller deposition 1/11/16, p 261, L. 21-24

[REDACTED]

216.

[REDACTED]

217.

[REDACTED]

[REDACTED]

<sup>244</sup> BPV-FULLER-0000221

<sup>245</sup> Fuller deposition 1/11/16, p. 271-272, L.24-22

<sup>246</sup> Fuller Exhibit 127

<sup>247</sup> Fuller Exhibit 138

218.

[REDACTED]

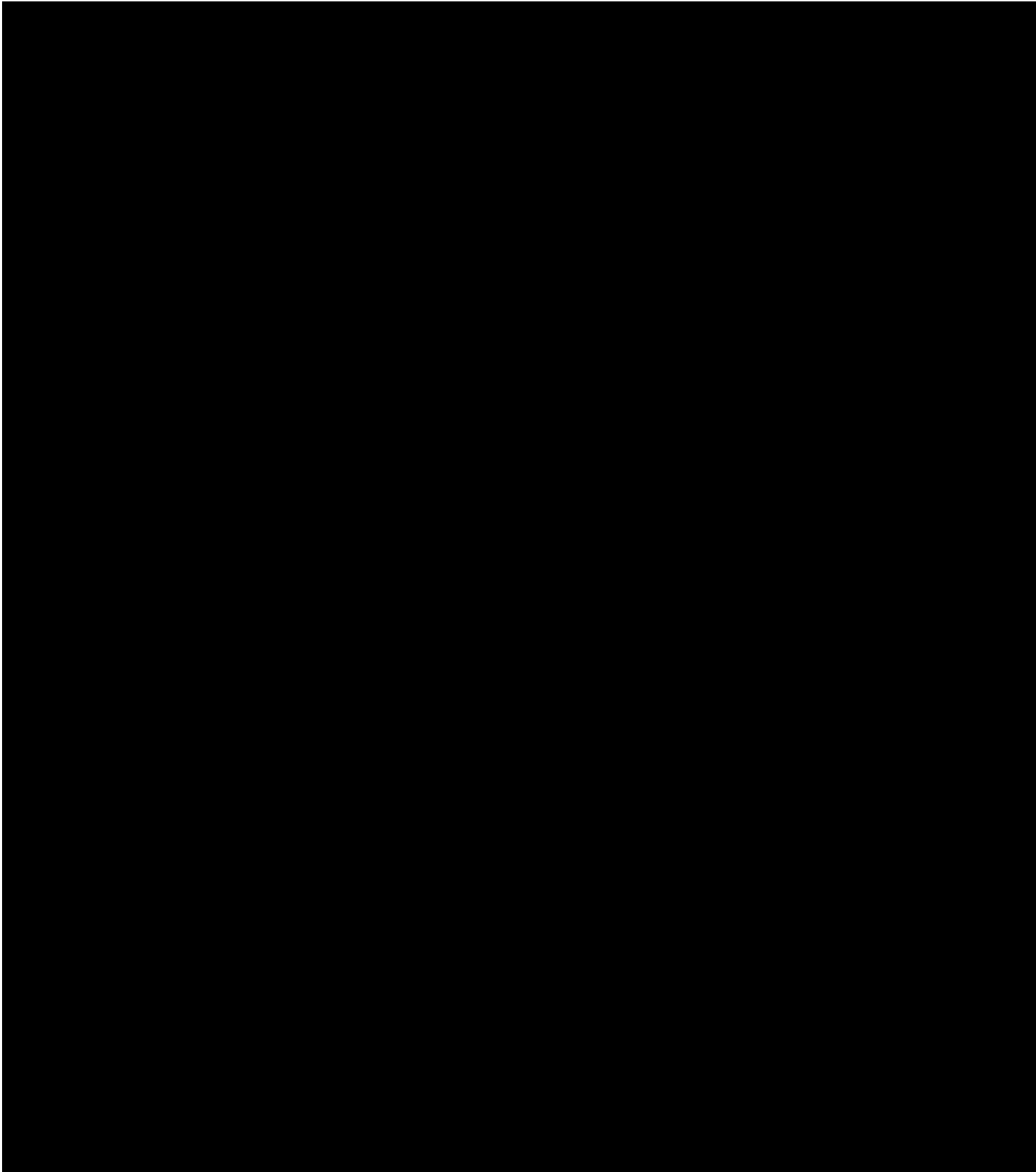
219.

[REDACTED]

220.

221.

[REDACTED]



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<sup>248</sup> Fuller Exhibit 138

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<sup>249</sup> Fuller Exhibit 138

<sup>250</sup> Fuller deposition 1/11/16, p. 134-135, L. 8-13

224.

[REDACTED]

[REDACTED]

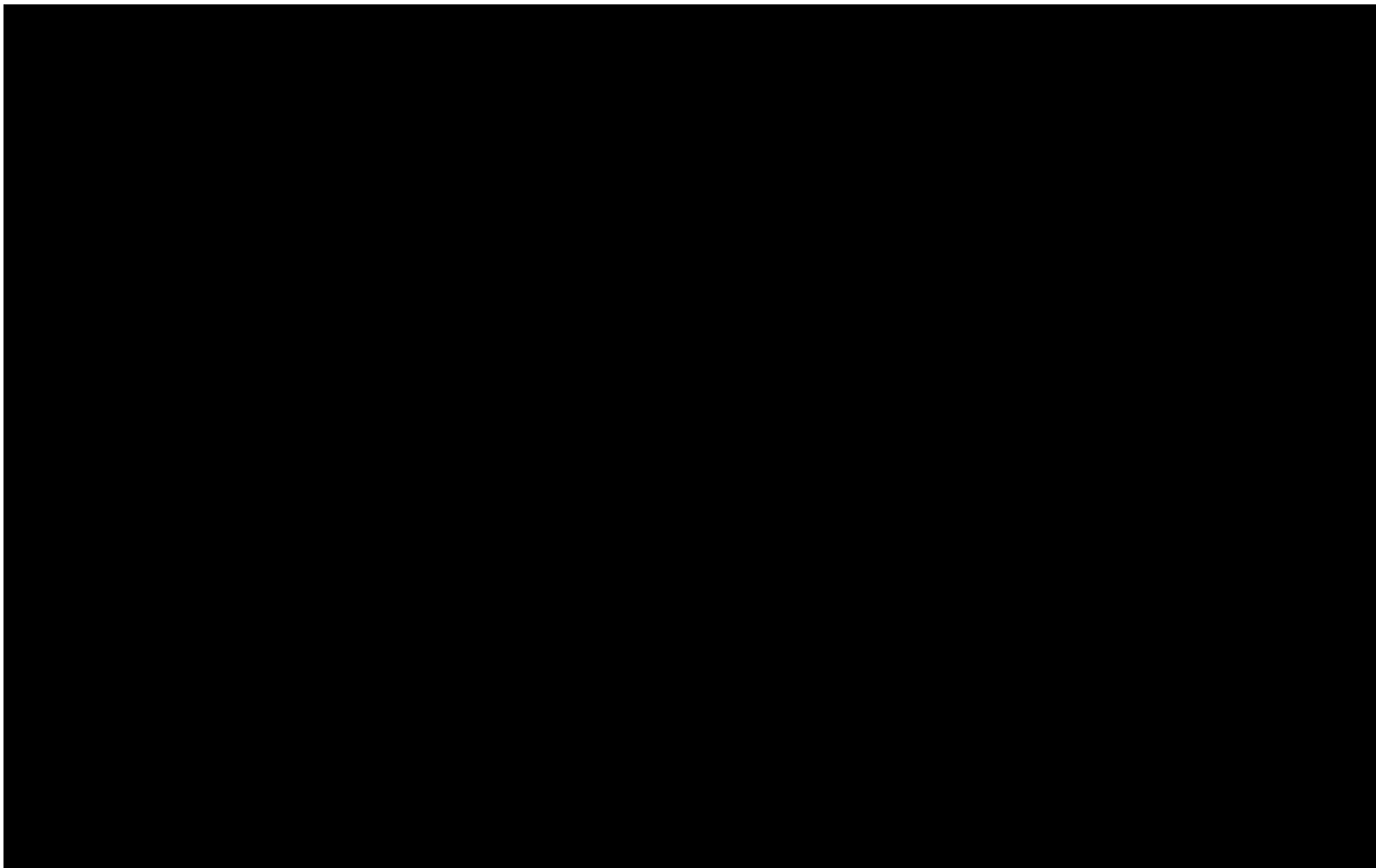
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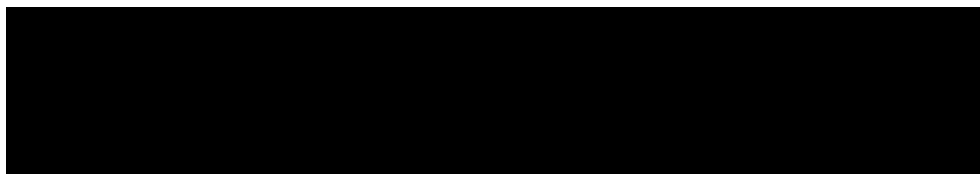
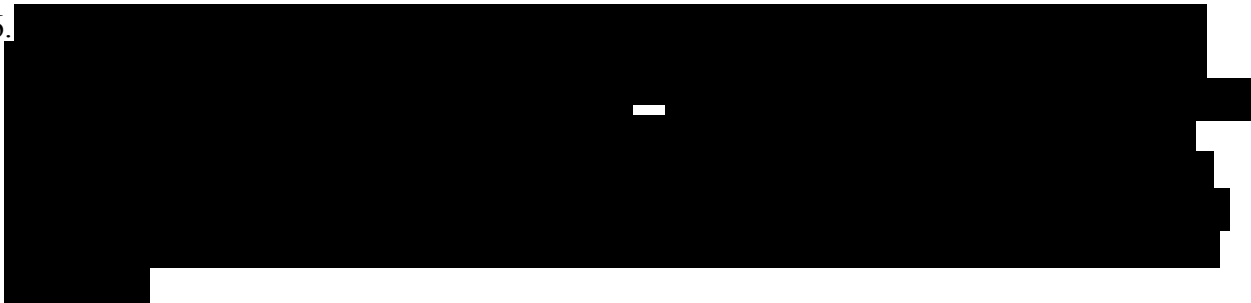
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<sup>251</sup> Fuller Exhibit 138; Poster

<sup>252</sup> Fuller Exhibit 138



226.



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<sup>253</sup> Fuller Exhibit 138

<sup>254</sup> Fuller Exhibit 138

<sup>255</sup> Simon M. Rabkin DJ, Kleshinski S, Kim D, Ransil BJ, Comparative evaluation of clinically available inferior vena cava filters with an in vitro physiologic simulation of the vena cava. Radiology. Dec 1993, 189(3), at 769-74

[REDACTED]

227.

[REDACTED]

[REDACTED]

228.

[REDACTED]

[REDACTED]

229.

[REDACTED]

[REDACTED]

[REDACTED]

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<sup>256</sup> Fuller Exhibit 138 K022236 p BPV-17-01-00057972

<sup>257</sup> Fuller Exhibit 138

<sup>258</sup> Fuller Exhibit 138

<sup>259</sup> Fuller Exhibit 138

230. [REDACTED]

231. [REDACTED]

232. [REDACTED]

[REDACTED]

[REDACTED]

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<sup>260</sup> Fuller Exhibit 138, K022236 at page BPV-17-01-00057973-4

<sup>261</sup> BPV-17-01-00002650

<sup>262</sup> BPV-17-01-00002650

<sup>263</sup> BPV-17-01-00002650

233.

[REDACTED]

[REDACTED]

234.

[REDACTED]

[REDACTED]

235.

[REDACTED]

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<sup>264</sup> BPV-17-01-00002650

<sup>265</sup> See Altrans Review of Filter Failure for Bard

[REDACTED]

236. [REDACTED]

237. [REDACTED]

[REDACTED]

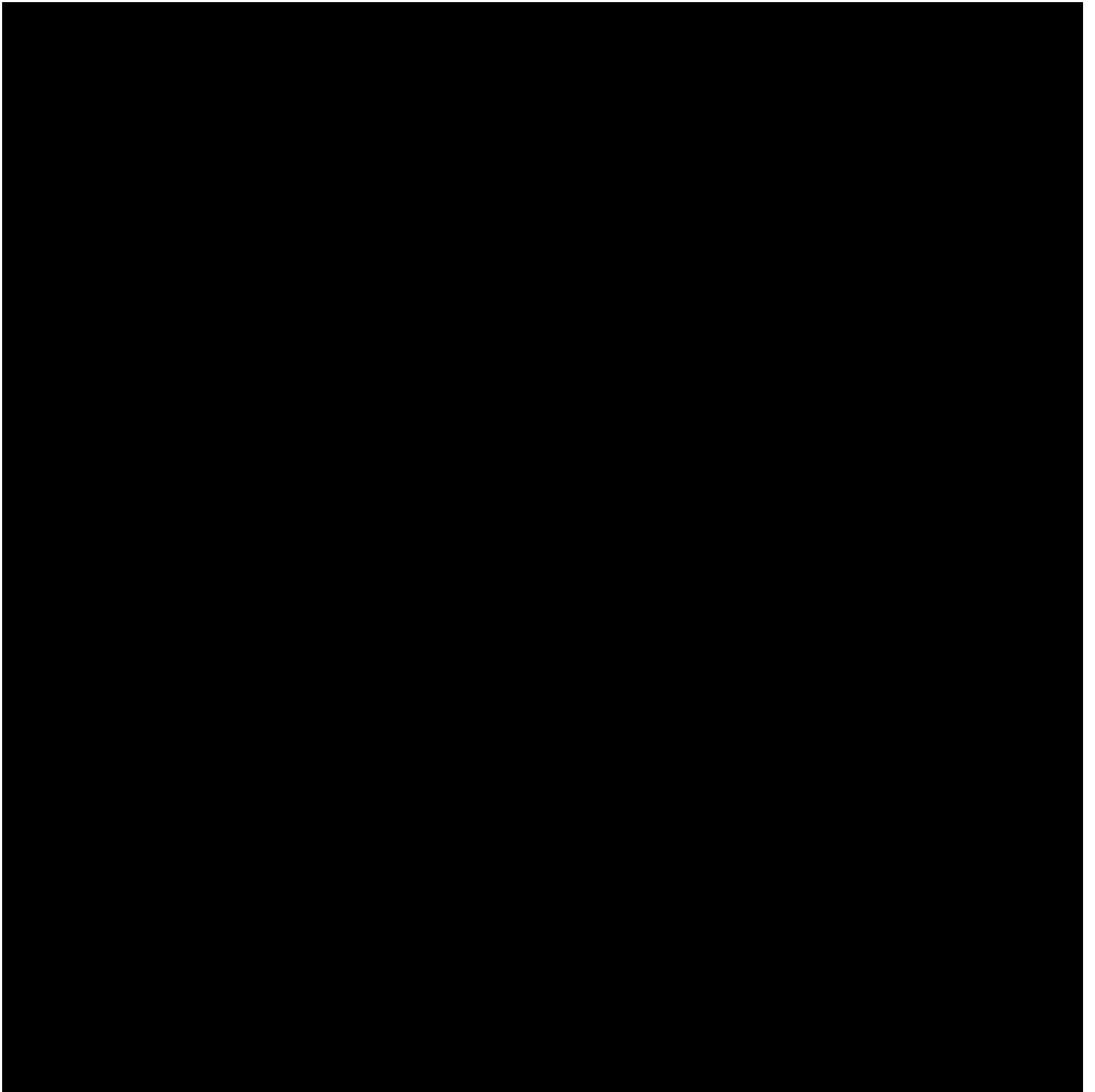
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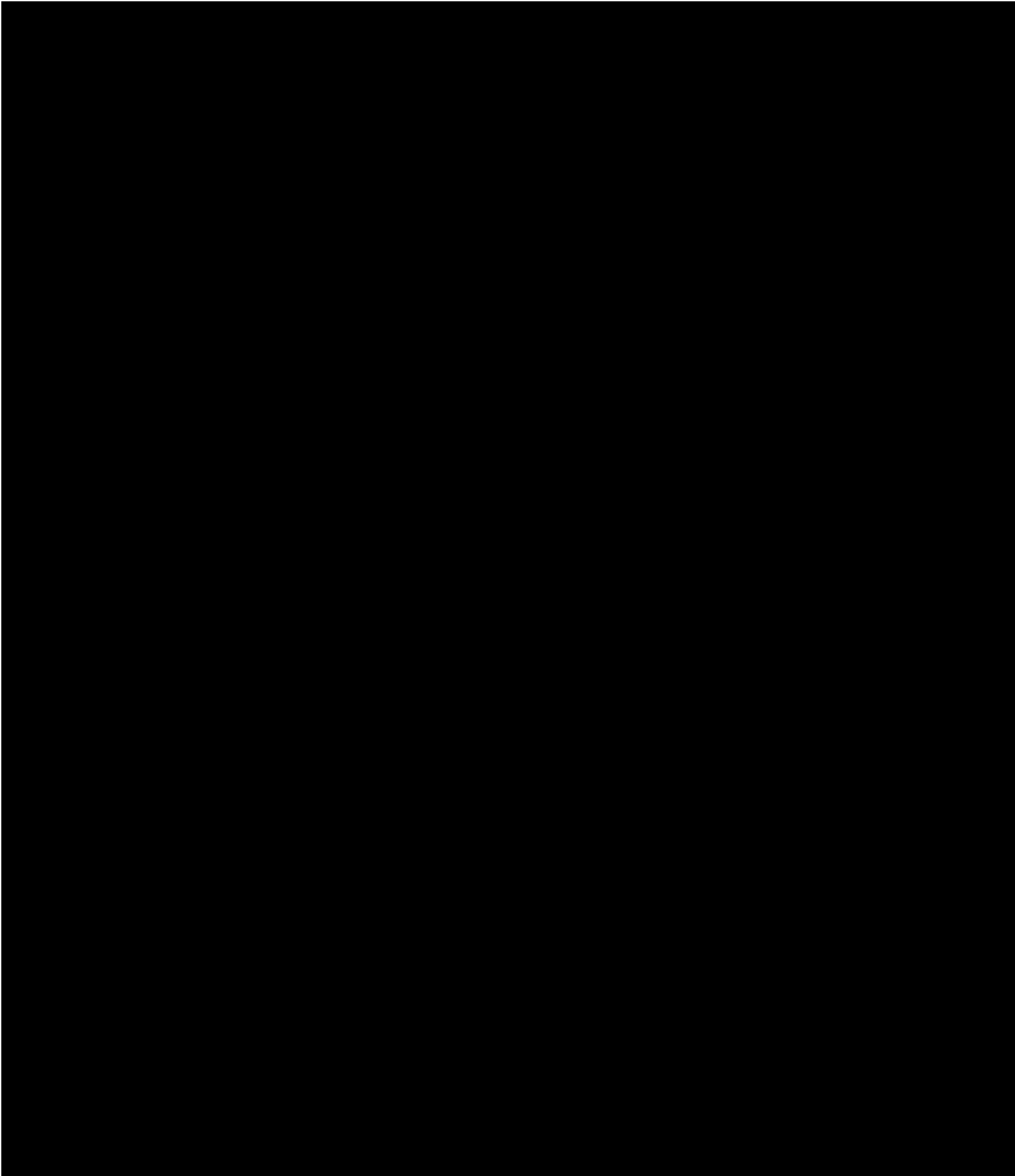
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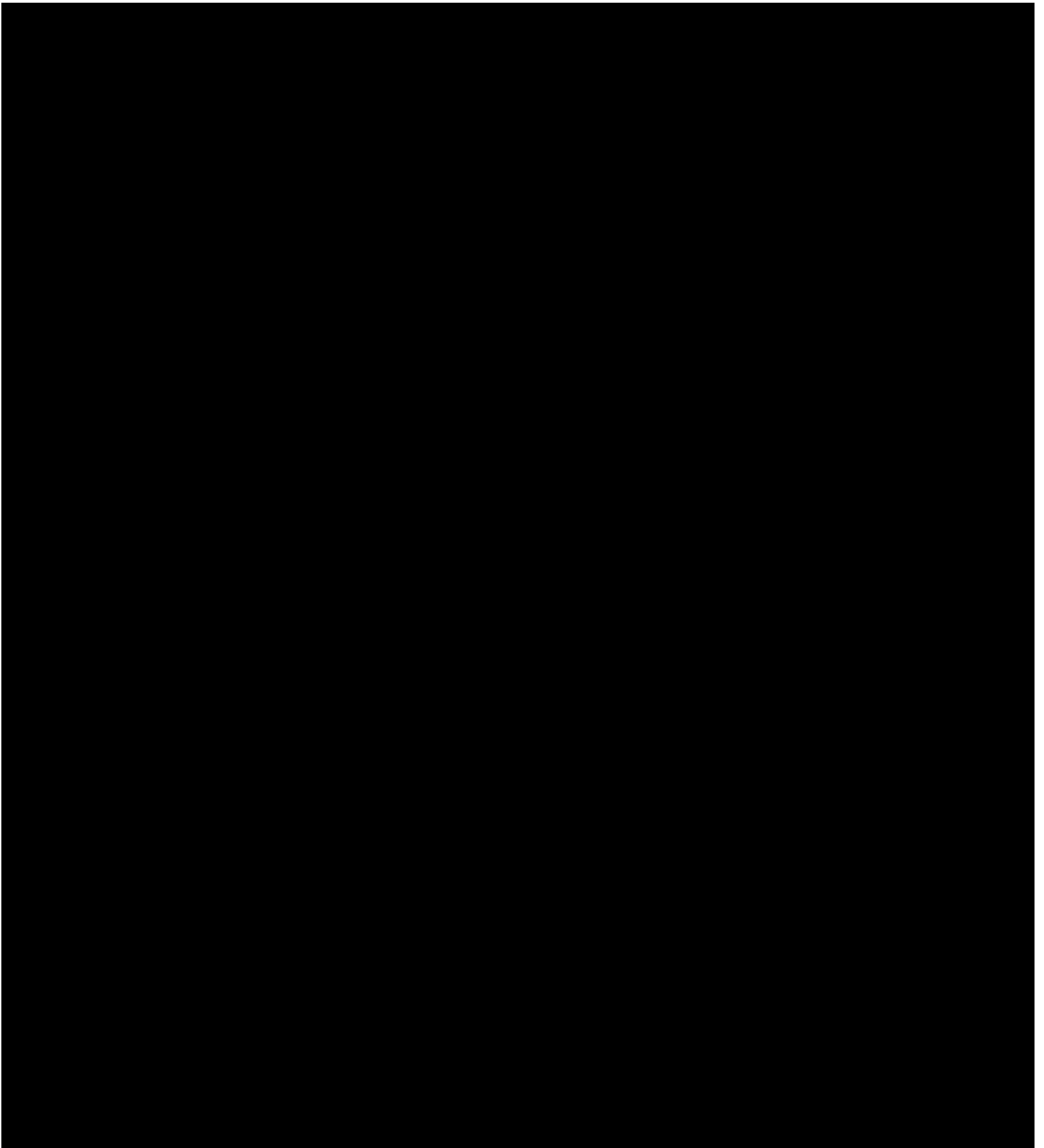


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<sup>269</sup> BPV-17-01-00058992







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<sup>270</sup> BPV-17-01-00051623.

[REDACTED]

241. [REDACTED]

242. [REDACTED]

[REDACTED]

243. [REDACTED]

[REDACTED]

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<sup>271</sup> Fuller deposition 1/11/16, p. 118-119

<sup>272</sup> Fuller deposition 1/11/16, p. 119, L. 7-19

<sup>273</sup> RD-RPT-099 August 4, 1999

<sup>274</sup> Fuller deposition 1/11/16, p. 135-138, L. 22-4, see Fuller Exhibit 127

[REDACTED]

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<sup>275</sup> Fuller deposition 1/11/16, p. 122-124, L.17 -14

<sup>276</sup> Fuller deposition 1/11/16, p. 125, L. 6-22

<sup>277</sup> Fuller deposition 1/11/16, p. 127-128, L. 23-7

<sup>278</sup> BPV-17-01-00057926

<sup>279</sup> BPV-FULLER-00002320

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302. [REDACTED]

303. [REDACTED]

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<sup>350</sup> BPV-17-01-00055242

<sup>351</sup> *Id.*

304. [REDACTED]

305. [REDACTED]

[REDACTED]

306. [REDACTED]

307. [REDACTED]

[REDACTED]

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<sup>352</sup> *Id.*

<sup>353</sup> *Id.*

<sup>354</sup> *Id.*

<sup>355</sup> *Id.*

<sup>356</sup> *Id.*

308. [REDACTED]

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312. [REDACTED]

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[REDACTED]

1-161 days) showed that the Recovery Filter may be safely retrieved and that the benefit of the procedure outweighs the potential associated risk.

**3. FDA's ODE reviewer's official summary to K031328's file regarding support of clearance of the RNF's retrieval option IFU.**

313. On July 24, 2003, FDA's ODE Reviewer Lisa Kennell, Microbiologist, summarized her review and her "understanding" of the RNF Retrieval Option for the RNF K031328 file.<sup>359</sup>

314. From the clearance of K022236, she understood the following 2002 modifications were made from the SNF to the RNF (Ms. Kennell included the heart symbols). RNF was already a FDA cleared product, substantially equivalent to SNF, able to be commercially marketed as a permanent IVC Filter:

*The modification to the intravascular filter are:*

♥*The wire diameter has been reduced from 0.014" to 0.013"*

♥*The closed dome shape (petal-like dome) has been changed to an open design*

♥*One sleeve that holds the filter wires to the body of the filter has been eliminated; and*

♥*The hooks that engage in the vena cava wall have been tapered.*

315. Ms. Kennell continued that in 510(k) K031328, "the firm provides data to substantiate the temporary indication and removal of the statement, including in vitro, animal and clinical information."<sup>360</sup>

**a. Animal Study**

316. For the animal study, Dr. Omar Hottenstein had reviewed Bard's data. A total of 18 sheep placed into one of four experimental groups. There were 18 animals but 24 filters placed:

Group	Retrieval Time	Healing Time Post Retrieval
A	Immediate	None
B	Immediate	3 weeks
C	12 weeks	None
D	12 weeks	8 weeks

<sup>361</sup>

317. All 24 filters were successfully removed intact (no fractures) and without clot or other aggregates. Cavograms revealed slightly caudal migration in 4 (17%), tilting in 6(25%). Group A

<sup>359</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

<sup>360</sup> BPV-17-01-00054098; FDA\_Production\_00001203,

<sup>361</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

and B grossly explanted tissue normal. For the group with 12 weeks implant, Group C and D, there are scattered small nodules on the adventitial surface in the region of the hooks, lines corresponding to the arms of the filters and areas of thickening and nodularity at the hook interface. There was evidence of transmural hemorrhages in Groups C and D, with D<C. According to Dr. Hottenstein: “The most interesting, and unexplainable, finding was the formation of lesions on the aorta at sites analogous lesions of the adjacent IVC. There was no gross evidence of retroperitoneal hemorrhage or communication between the vessel lumens.” He continued: “The hypothesis for these aortic lesions was the relatively small mean diameters of the IVC in sheep (10.8-13.9) mm in two animals with full thickness aortic lesions). The filter is designed for use in humans, with IVC diameters averaging 21 mm in diameter up to 28mm diameter vessels.”<sup>362</sup>

#### **b. Dr. Asch and Associates- Clinical Data**

318. The clinical data was again obtained from Dr. Asch but also with two of Dr. Asch’s colleagues at six Toronto area hospitals with data provided for 58 filters. Of the 58 filters implanted, a total of 46 were retrieved (79%), 8 remained in place, and 4 patients (7%) died with filters in place from causes thought unrelated to filter placement and/or retrieval. Time to removal of the 46 filters ranged from 1 to 161 days, average 60 days. Patient follow-up post retrieval was an average of 325 days. Two methods described in the IFU were used to retrieve the filter in all but 4 cases (9%), when a larger sheath was used, or a snare loop was attempted instead of using the Recovery Cone. There was one case of PE reported to occur when using the larger sheath (3%). The only other adverse event reported was a fractured filter arm and hook (\*previously reported under K022336- Pt 33 of the Asch 2000 study). Ms. Kennell wrote about that patient based on the information provided to her by Bard: “*The fracture was believed to be secondary to stresses due to delivery and placement infrarenally, causing severe deflection and embedding of the hook into the boney tissue of the vertebrae. The filter was retrieved, minus the hook.*”<sup>363</sup>

319. Bard for the retrieval indication continued to rely on Dr. Asch study but as a result of interaction with FDA, expanded the population to include two other Toronto colleagues. Dr. Asch supplied patient information about 27 RNF filters he retrieved (59%) for K02236 in a population of 35 patients to clear RNF as a permanent filter. For K031328 the population was 58 with 46 filters removed by Dr. Asch and colleagues to support K031328 as a retrievable filter. The majority of filters studied by Dr. Asch were retrieved at 30 days (14, 30%). One filter was removed surgically during a cancer surgery where the mass was impinging the filter. Lisa Kennell in her summary did not reference that she had learned of the K02236 “migration report” for patient #9 (3%) in the Dr. Asch original population. She did not indicate she knew of reports of tilt or perforation reports. However, both were asked about in FDA’s letters for K02236.

320. As not accurately reported to Ms. Kennell and the FDA, beginning with K02236, Dr. Asch wrote the following clinical description of Patient 33 that was not provided in either Bard’s K02236 or K031328. It was also not included in Robert Carr’s May 2002 report or Bard’s July 9, 2002, “Failure Investigation Report” or apparently seen by Kay Fuller. Dr. Asch described that

<sup>362</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

<sup>363</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

this 29-year old woman's post-delivery CT scan of April 2, 2002 noted the malposition of the fractured filter arm as well as a suspicion of caval perforation of a leg. The patient's filter subsequently was found to have tilted approximately 15 degrees from baseline, a fractured filter arm fragment adjacent to the right renal vein. There was a possible perforation of the leg outside of the IVC on imaging. On retrieval by Dr. Asch, the fractured filter hook could not be found but which was thought to be "presumably" located at the site of caval perforation. Dr. Asch makes no reference to the hook in the vertebrae at time of retrieval as occurs only in NMT and Bard's reports. This one patient #33 had shown tilting, migration of arm and possibly hook fractures and leg perforation. Dr. Asch wrote in his report that he considered the patient as having a "fractured filter" and it was reported back to both the distributor (Bard) and the manufacturer (NMT) in April 2002:

*I did contact the filter distributor and manufacturer to inform them of the filter fracture today. I will make arrangements for the filter to be shipped back to the manufacturer for evaluation. HPB, and the Hospital Ethics Board were informed of this condition.* <sup>364</sup>

321. Ms. Kennell does not document that she was fully informed about Dr. Asch's patient data as described in the Clinical Study April 2000 poster summary: 'Clinical Trial' the data was for 35 implanted patients, with 27 filters (77.1%) with filters removed, 3 (11%) had 1-2 legs incorporated into the caval wall; 1 (4%) had transmural incorporation, 1 (4%) had a filter leg seen outside the vessel lumen, 1 (4%) had questionable caval narrowing at the filter site, 1 (4%) with mild caval stenosis, 1 (4%) with increased tilt from the baseline with slight penetration of the wall, 1 (4%) migration of 4 cm, 1(4%) filter arm fracture with missing leg hook.<sup>365</sup> These were no reports of "deployment issues" related to over-polishing of the spline and the subject of subsequent manufacturing changes.

322. Ms. Kennell does not record she was provided the draft Bard report for Patient 33, which had been seen by Kay Fuller, regarding a report of an acute fracture of the hook at time of retrieval: "*during the removal procedure, the small hook fractured and remained in this tissue, although it is not visible with available equipment.*" Viewing this draft report, Ms. Fuller, the Regulatory Specialist had written next to that statement "*Is this true/accurate?*"<sup>366</sup> Ms. Fuller was aware that this report showed a (3% filter arm and hook fracture) and 3% migration for a small clinical study.<sup>367</sup>

323. Ms. Kennell continued that in K031328 Bard proposed to remove the restriction in the label for retrieval, as well as to add instructions for removal. The indication statement is also revised with the following addition:

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<sup>364</sup> Fuller Exhibit 121

<sup>365</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140; BPV-17-01-00057953

<sup>366</sup> Fuller deposition 2016, p 100-104 L 6-17

<sup>367</sup> *Id.*

*Recovery filter may be removed according to the instructions supplied in the Section labeled: Optional Procedure for Filter Removal. Data from removal in a 58-patient study suggests that the device can be safely removed (mean of 60 days, range 1-161 days).<sup>368</sup>*

**c. Recovery Cone**

324. Ms. Kennell wrote that the “Recovery Cone Removal System” is apparently to be supplied separately, and is the device to facilitate removal. She made no note that she asked for documentation or received documentation about the clearance status of the Recovery Cone. Despite the lack of inclusion of the Recovery Cone in the 510(k) for clearance, there is a very clear warning in the IFU that “only the Cone Removal System should be used, and only when there is not significant thrombus trapped in the filter or embedded within the vena cava wall. The “Potential Complications” section does not mention recurrent pulmonary embolism if device other than the Recovery Cone are used, but this was observed in the clinical study. This implies to a physician that the RNF and the Recovery Cone have been created as a kit and that there has been testing and documentation developed regarding the ease of the Recovery Cone to retrieve the RNF. Despite the requested 510(k) clearance, Bard’s marketing would promote the use of the Recovery Cone at each retrieval. Ms. Kennell did not ask for valid evidence to support Bard’s making such a marketing claim and Bard also did not request clearance of such a claim.

325. Ms. Kennell said she discussed the proposed Bard label and retrieval issue with FDA’s Dr. Chaneysson. He agreed that this retrieval statement about the Recovery Cone should be added, as it is more important for the user to understand the ramifications of using an alternate device. In the Canadian compassionate use clinical trial, there had been one patient with a pulmonary embolus released without use of the Recovery cone.<sup>369</sup>

326. Other items included in the Abbreviated 510(k), according to Ms. Kennel’s summary were a mandatory 510(k) summary from Bard, an indication for use statement, and a signed “Truthful and Accurate Statement,” as well as items requested during Bard/FDA’s pre-submission meeting. The 510(k) was documented as containing the financial disclosure statements and procedural notes taken for the clinical patients.<sup>370</sup>

327.

**d. Use of Abbreviated 510(k) which Bridges K022236**

328. Ms. Kennell continued that since this 510(k) is identified as an abbreviated 510(k), she could not determine the exact reason for considering it an abbreviated submission because she could not find any Bard reference to standards used for the device beyond reference to the FDA’s Guidance mentioned on page 31. Ms. Mary Edwards, the FDA contact (now that Ms. Fuller had left Bard), verified to Ms. Kennell that all the information contained in K022236 (RNF substantially

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<sup>368</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

<sup>369</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

<sup>370</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

equivalent to SNF) was referenced for K031328 including the standards.<sup>371</sup> Indirectly, Bard was certifying to FDA and Ms. Kennel that between K022236 and K031328 all the standards referenced had been met. That would include the ASTM standards which required “finished device testing.” Ms. Kennel was told by Mary Edwards that Bard had chosen to reference the information in its Special 510(k) K022236 rather than to duplicate the information for the abbreviated 510(k). Ms. Kennel indicated she looked at the earlier Special 510(k) submission K022236 to look at bench and animal testing done by Bard to support the 510(k) clearance of RNF as a Design Modification of SNF as a substantially equivalent permanent IVC Filter.<sup>372</sup>

**e. Reference to “Anonymous Tipster.”**

329. Ms. Kennel, wrote in her summary about her “*understanding*” about the receipt of an “anonymous tip” issue (which may or may not represent Kay Fuller’s phone call to Dr. Harvey). Ms. Kennel put into the official 510(k) record for FDA her appreciation of the issue from a “tipster”:

*An anonymous tip was received alleging that the device was not assessed for shelf life, so I requested that this data be submitted. I reviewed the data, submitted by fax, and, and found it to substantiated a 3-year shelf life. I believe the reason the tipster communicated concern about the issue was that there were failures in the first round of testing, which necessitated modification of processing methods. After modification, the acceptance criteria were met for each parameters.*<sup>373</sup>

330. There was clearance on July 25, 2003 for Bard to market the RNF for a new retrieval option. Ms. Fuller’s two-tiered strategy for obtaining clearance of a retrievable filter had been successful for bringing a commercial RNF IVC filter to the United States market for Bard. Ms. Fuller was no longer working at Bard to share in Bard’s victory with Mary Edwards, and Bard’s corporate management and Marketing.

**C. An audit finds that Bard adopted NMT’s RNF testing and results without any further design verification and validation.**

331. Design history records and files must be maintained as part of daily business by manufacturers for medical devices that it manufactures and commercially sells in the United States. These device history document documents are part of required Good Manufacturing Practices of the Quality System Regulations<sup>374</sup> and are intended to be available for review by regulatory agencies, including the FDA, at time of facility inspections. The documents are to show the company’s

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<sup>371</sup> Fuller deposition 2016, p 100-104 L 6-17

<sup>372</sup> *Id.*

<sup>373</sup> BPV-17-01-00054098; FDA\_Production\_00001203; Fuller Exhibit 140

<sup>374</sup> 21 CFR part 820

commitment to adherence to adequate quality practices and implementation of adequate controls for medical devices to support continued safety and efficacy.

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341. Bard's Recovery IVC filter also failed to account for the changing environment of a patient's IVC, particularly when promoting its use in morbidly obese patients undergoing the pressure changes of mechanical ventilation and surgery. This is an issue that was known to Bard or should have been known prior to marketing the Recovery for sale to the public, and it should have conducted pre-market testing to address the dynamic nature of the inferior vena cava. The 1999 Guidance for pre-1999 "permanent" filters noted that the walls of the vena cava are known to move with patient's respiration and that changes in intra-abdominal pressure induce flexion on the limbs of the filter. Bard did no known study or analysis of its retrievable IVC filters to address this concern.

342. The 1999 Guidance indicated that filter migration in either the caudal or cephalic direction did not appear to be associated with clinically significant events in permanent filters, but that pre-1999 FDA assumption was contradicted by the post-market performance of the Recovery Filter. This change in the anticipated performance of Bard's Recovery IVC filter from prior IVC filter models and particularly the SNF—which Bard was using as the Recovery's predicate device in the 510(k) process—should have raised a new safety signal to Bard to trigger questioning of the adequacy of its Recovery IVC filter design and production. The significance of this safety signal was further supported when Bard internally compared the performance of the Recovery to competitor's filters and the SNF. At all times, Bard had the ability to market to physicians the use of the SNF as an acceptable alternative permanent IVC filter.

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<sup>382</sup> BPV-17-01-00097816-7.

<sup>383</sup> Ronald Robinson, Division of Solid and Fluid Mechanics, Office of Science and Engineering Laboratories, CDRH, FDA BPV-17-01-00045862-( see -00045878)

<sup>384</sup> BPV-17-01-00098021

<sup>385</sup> US Patent No. 6,007,558 titled "Removable Embolus Blood Clot Filter" assigned on December 28, 1999. The inventors were Adrian Ravenscroft and Stephen Kleshinski. The assignee was NMT.

**D. Bard failed to adhere to pre-market and post-market requirements and standards as it starts to sell RNF**

343. Bard failed to use adequate design, testing and analysis, both pre-market and post-market functions of industry, for developing and marketing safe and effective Recovery Family of retrievable IVC filter substantially equivalent to predicate SNF. Bard's testing and analysis should have provided it with early notice before there was 510(k) clearance for marketing that the new RNF family of filters were not substantially equivalent to the SNF and created a greater potential risk for implanted patients. Yet, despite this notice, Bard's 510(k) consistently failed to adequately disclose to FDA's reviewers the increased risk compared to permanent filters. Also, Bard did not disclose to FDA's reviewers in its 510(k), Bard's internal plans to aggressively market its new Recovery Family of Filters to healthcare providers for new off-label expanded and unsupported indications. This aggressive off-label marketing by Bard should have been foreseeable that it increased the risk for injury and death for patients. Such promotions changed the intended use and not only misbranded the Bard filters but would result greater harm to the public. Because of Bard's marketing, patients would be implanted prophylactically and outside the cleared indications of grandfathered pre-1976 predicates. The use of the filters, the risk versus benefit determination and the intended use was changed by Bard without providing physicians with adequate instructions for use or warnings. 21 CFR § 801.4.
344. Bard's marketing inaccurately represented to prescribers and providers that its Recovery Filters were safe and suitable for the new indication of 'retrieval' as well as permanent implantation before it was even cleared to promote Recovery for a retrieval indication. Bard's Marketing indicated removal of the filter was an option based solely on the physician's preference and not based on science or testing of the design of its filters. Patient brochures informed patients that there was no need to get the filters retrieved, they could remain permanently.
345. Bard Marketing, not the FDA clearance, indicated to healthcare providers that its RNF was able to be retrieved using Bard's Recovery Cone despite not having not obtained FDA's clearance for marketing of the accessory for the Bard Recovery Family of products and Bard's internal knowledge from study before 510(k) clearance that retrieval was difficult and not predicted by use of the Recovery cone. Bard failed to adequately warn healthcare providers of the difficulties associated with IVCF removal, device instability, tendency to tilt or migrate, as well as the risks of fracture and embolization, including reports of sudden death.
346. Bard promoted its permanent Recovery IVC filters cleared as durable enough for permanent placement in patients yet flexible enough to be retrieved at any time by a physician. However, Bard did not notify users that it had failed to conduct adequate testing and studies necessary to support these marketing claims. Bard made these claims despite knowledge of post-market analyses after launch of the Recovery filter showed that it had serious risks of movement, fracture, and death as well as difficulties with retrieval.<sup>386</sup>

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<sup>386</sup> Hull JE, Robertson SW. Bard Recovery Filter: evaluation and management of vena cava limb perforation, fracture, and migration. Nicholson W, et al., Prevalence of Fracture and Fragment Embolization of the Bard Recovery and Bard G2 Cava, *J Vasc Interv Radiol*, 2009, 20(1) at 52-

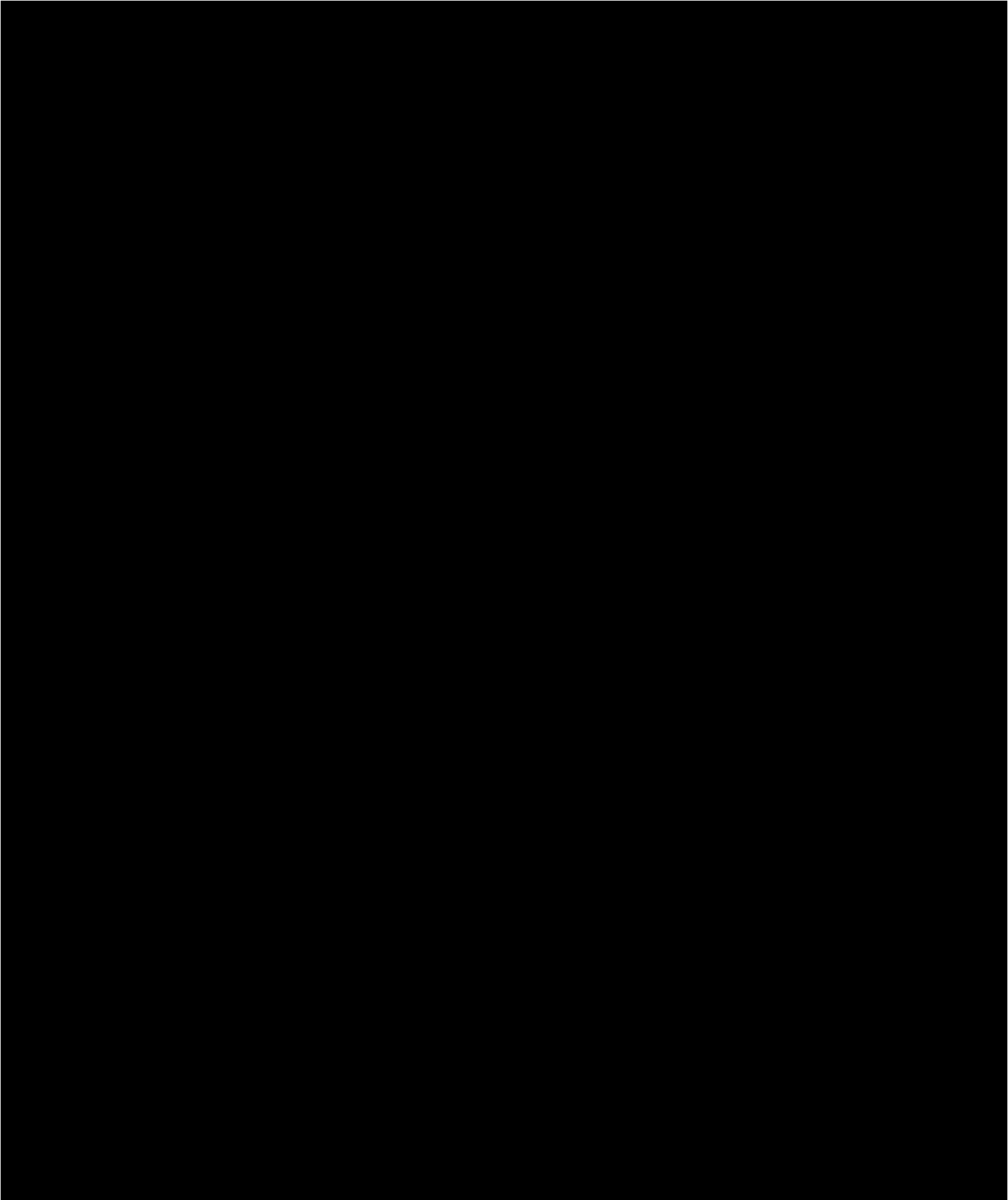
**IX. BASES OPINION #3: BARD'S ACTIONS FOR POST-MARKET OVERSIGHT CONTINUED TO PERMIT MARKETING OF THE FLAWED RNF AS A PERMANENT IVC FILTER**

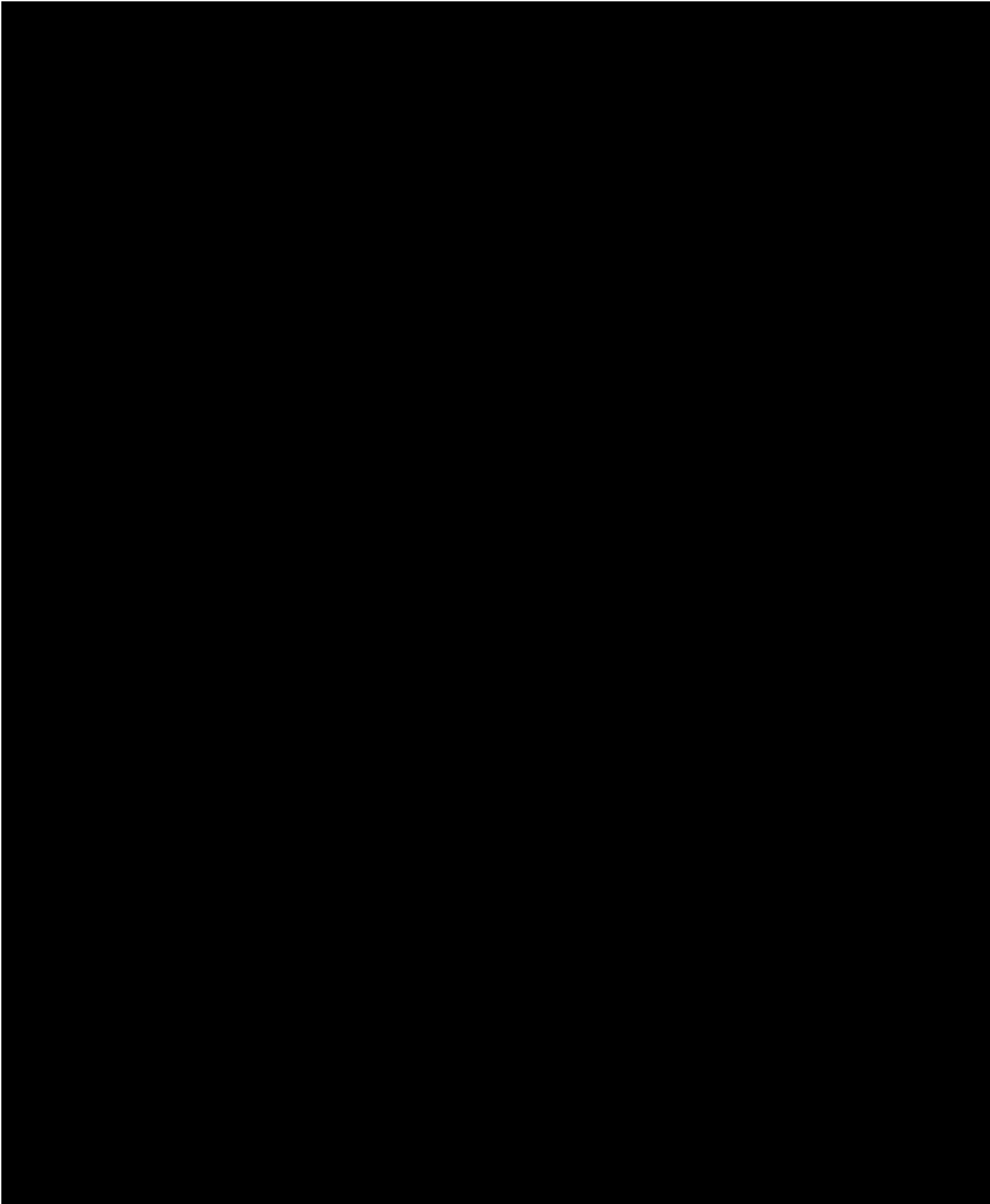
Despite obtaining RNF 510(k) clearance from FDA by asserting that the RNF was substantially equivalent to the SNF permanent IVC filter, Bard quickly learned that when the RNF was implanted in living patients it failed at much higher rates and produced significant complications much greater than occurred with the SNF. Despite the foreseeable risks for patients, Bard continued to sell the RNF without providing adequate warnings to physicians regarding the RNF's risks, the need to continue to monitor patients after implanted with the RNF, difficulties with retrieval, and the need to remove the RNF from a patient as soon as clinically feasible. Bard's marketing activities and plans downplayed the risks for implanted filters with device aging and overstated benefits to its sales force and physicians. Furthermore, Bard Marketing's off-label promotion expanded the population of patients implanted with the RNF into new and healthier patient populations beyond its cleared indications for use, while at the same time failing to protect and warn physicians and patients about the true risks of complications, reported failures, revision surgery and death with the RNF.

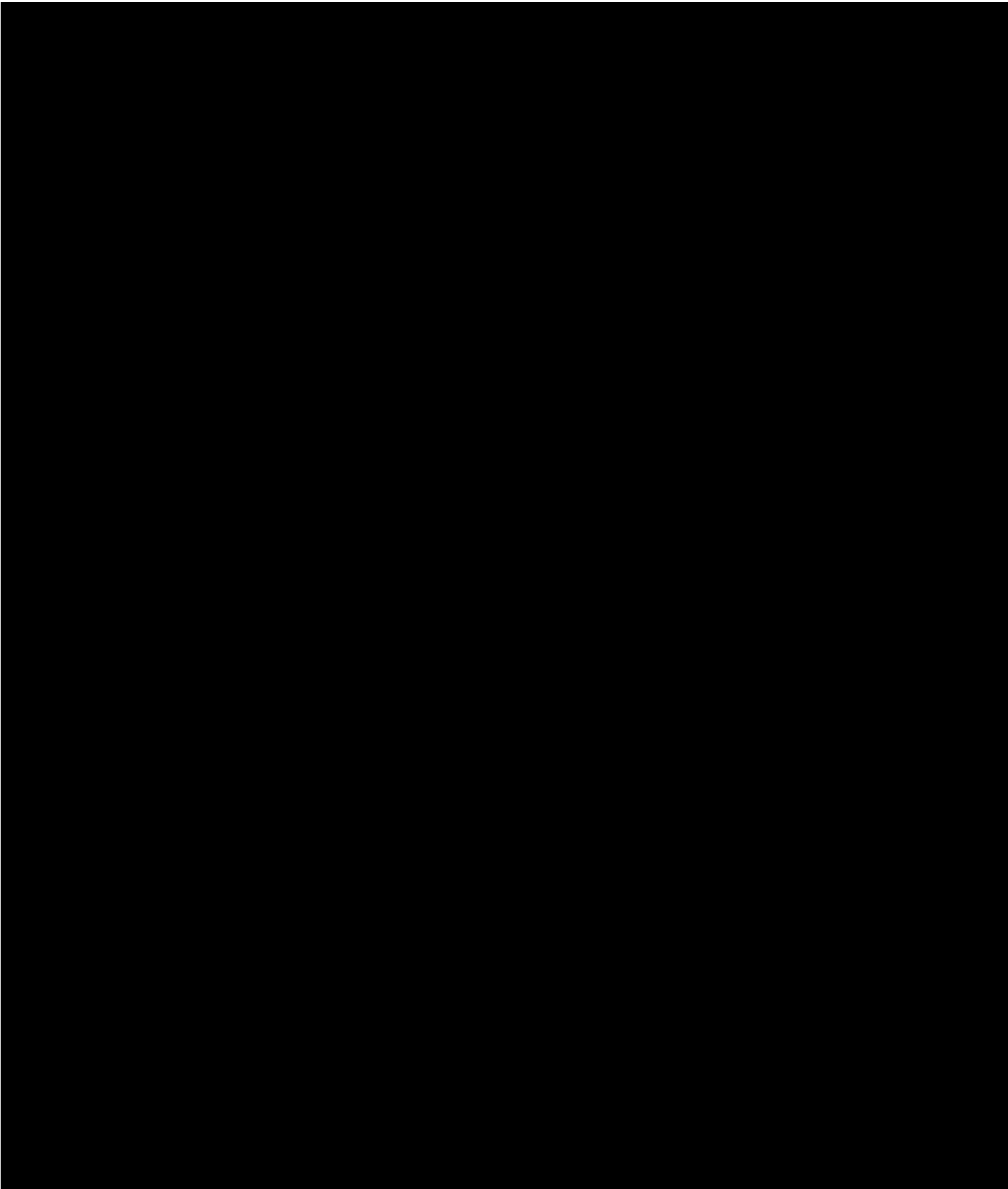
***Applicable Regulations:*** 21 USC § 331(a)(b); 21 CFR § 803; 21 CFR § 801.109; 21 USC § 352(a)(f)(1)(2)(t); 21 USC § 321(n); 21 USC § 351; 21 CFR part 7; 21 CFR part 820; 21 CFR § 806

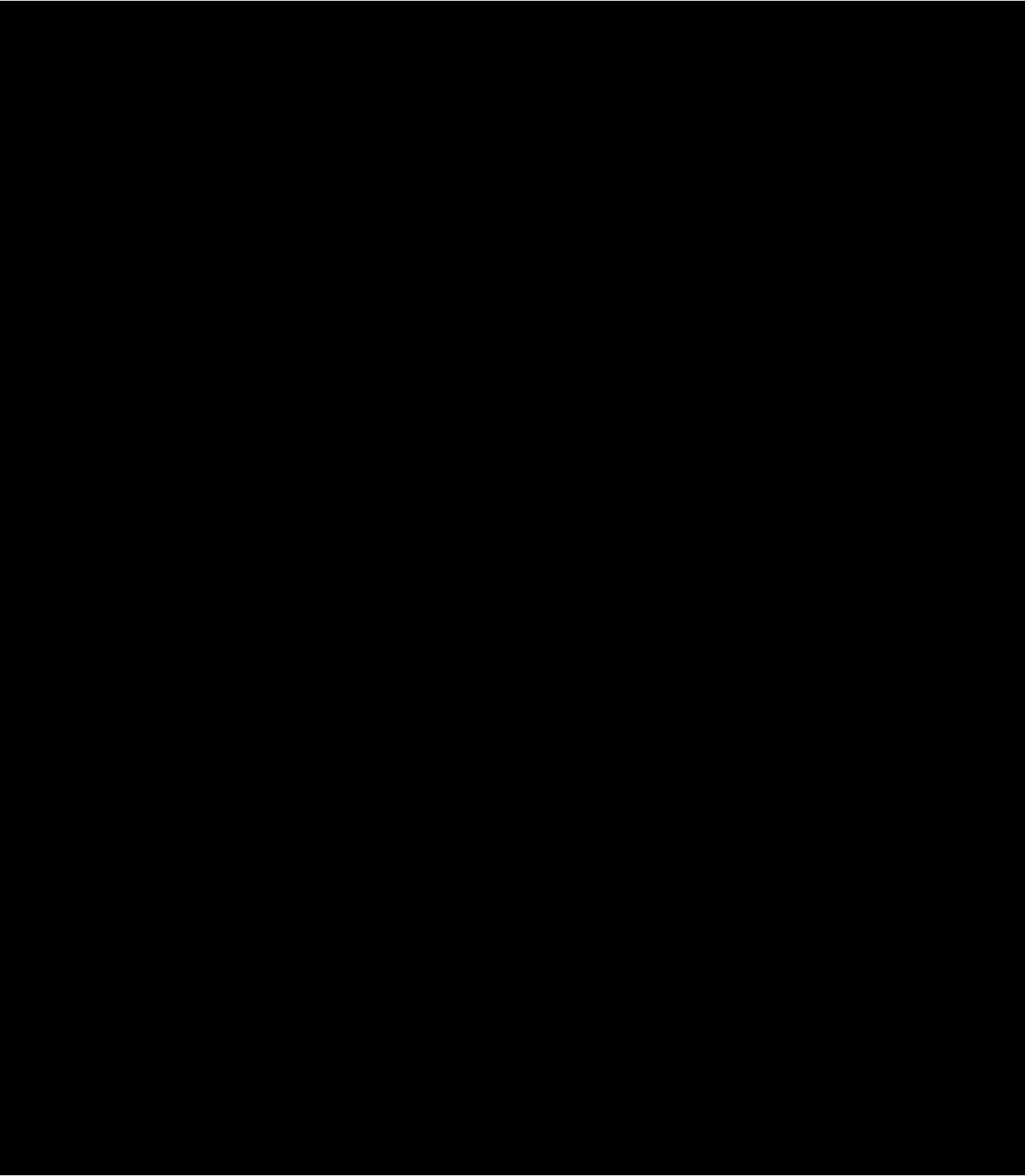
60. Filters and Clinical Implications Including Cardiac Perforation and Tamponade, *Arch Intr. Med*, Nov 2010, 170, at 1827-31. BPV-TRIAL-EXHIBIT-0762

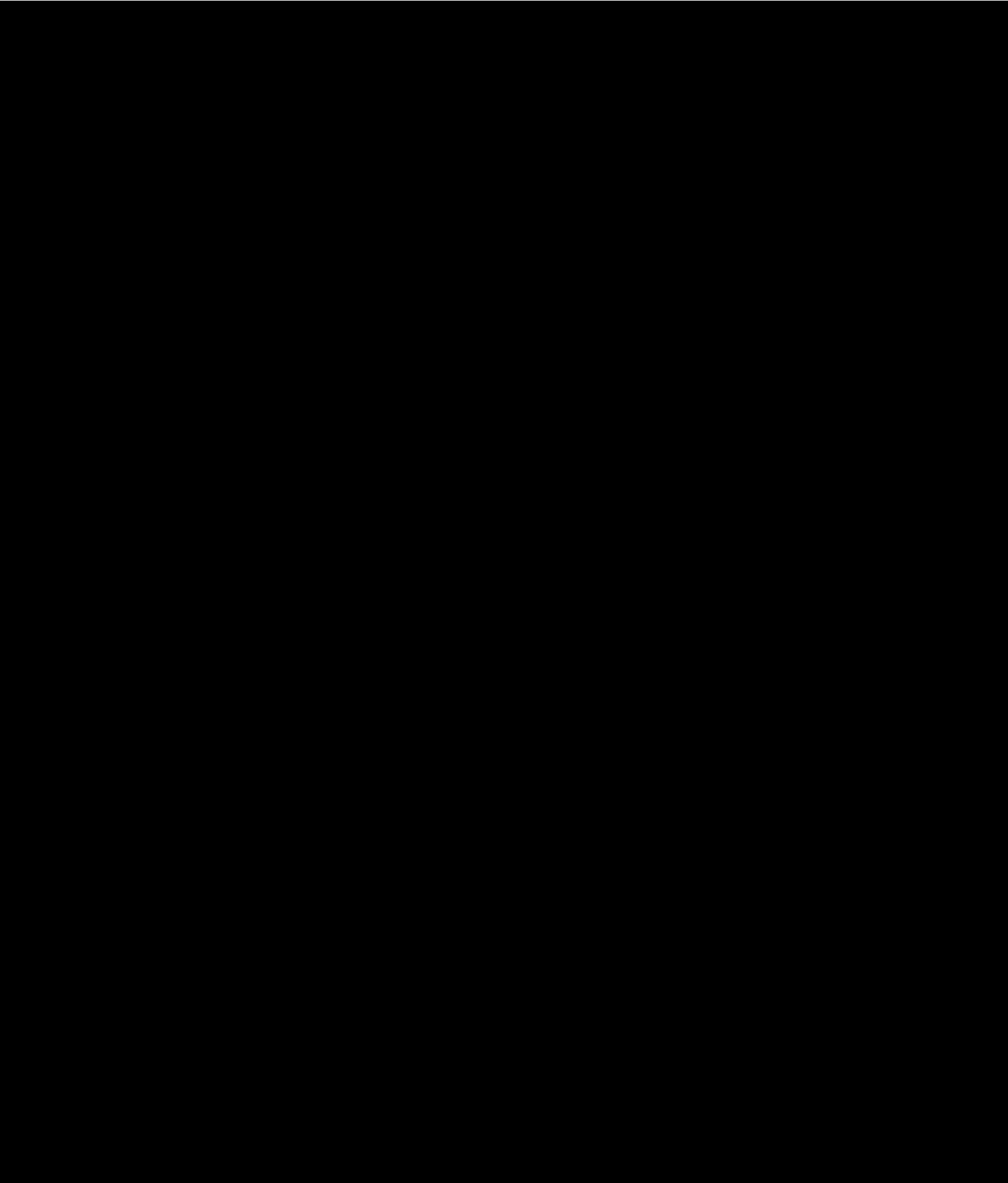
<sup>387</sup> BPVE-01-00511127; BPVE-01-00511131

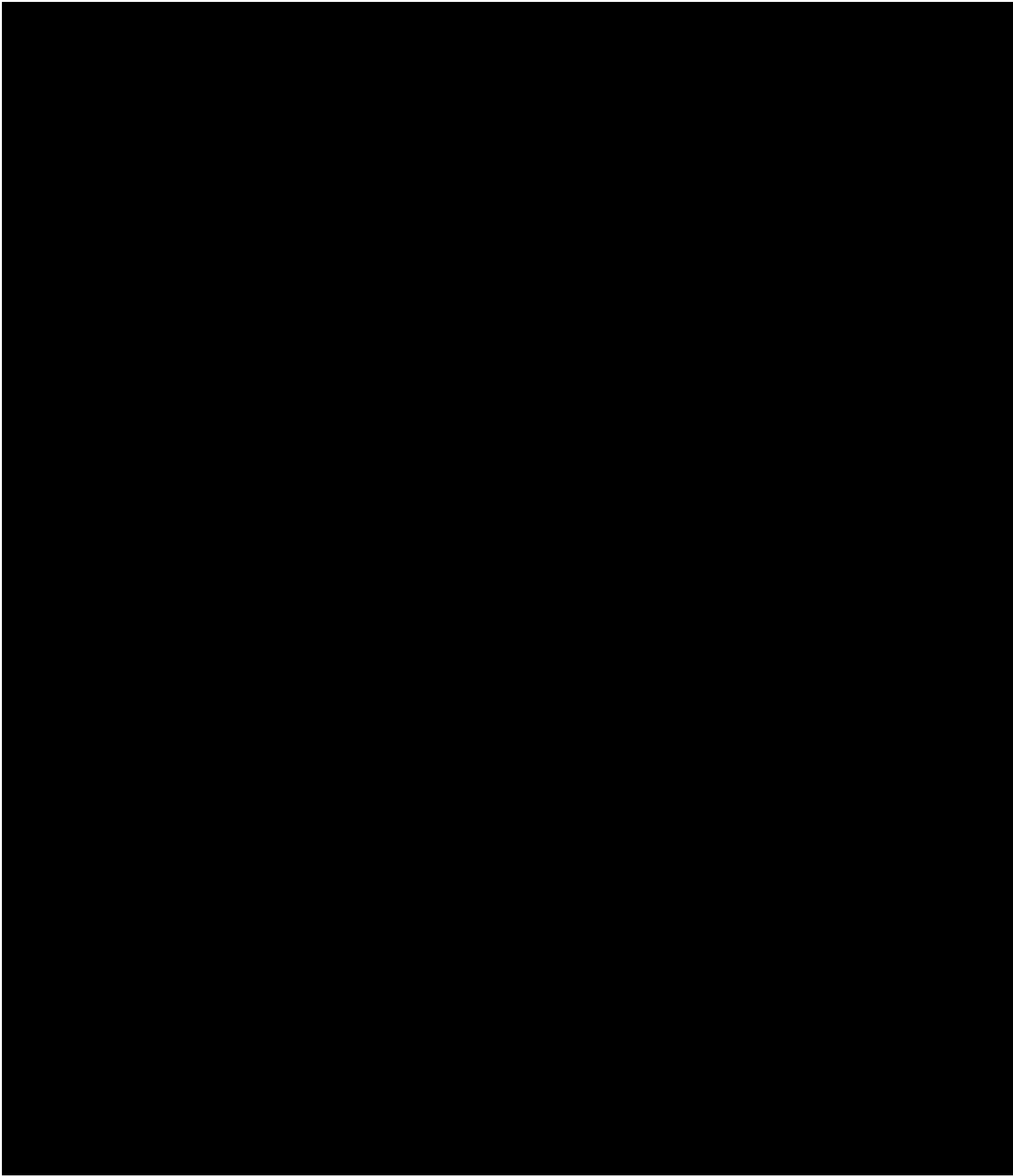




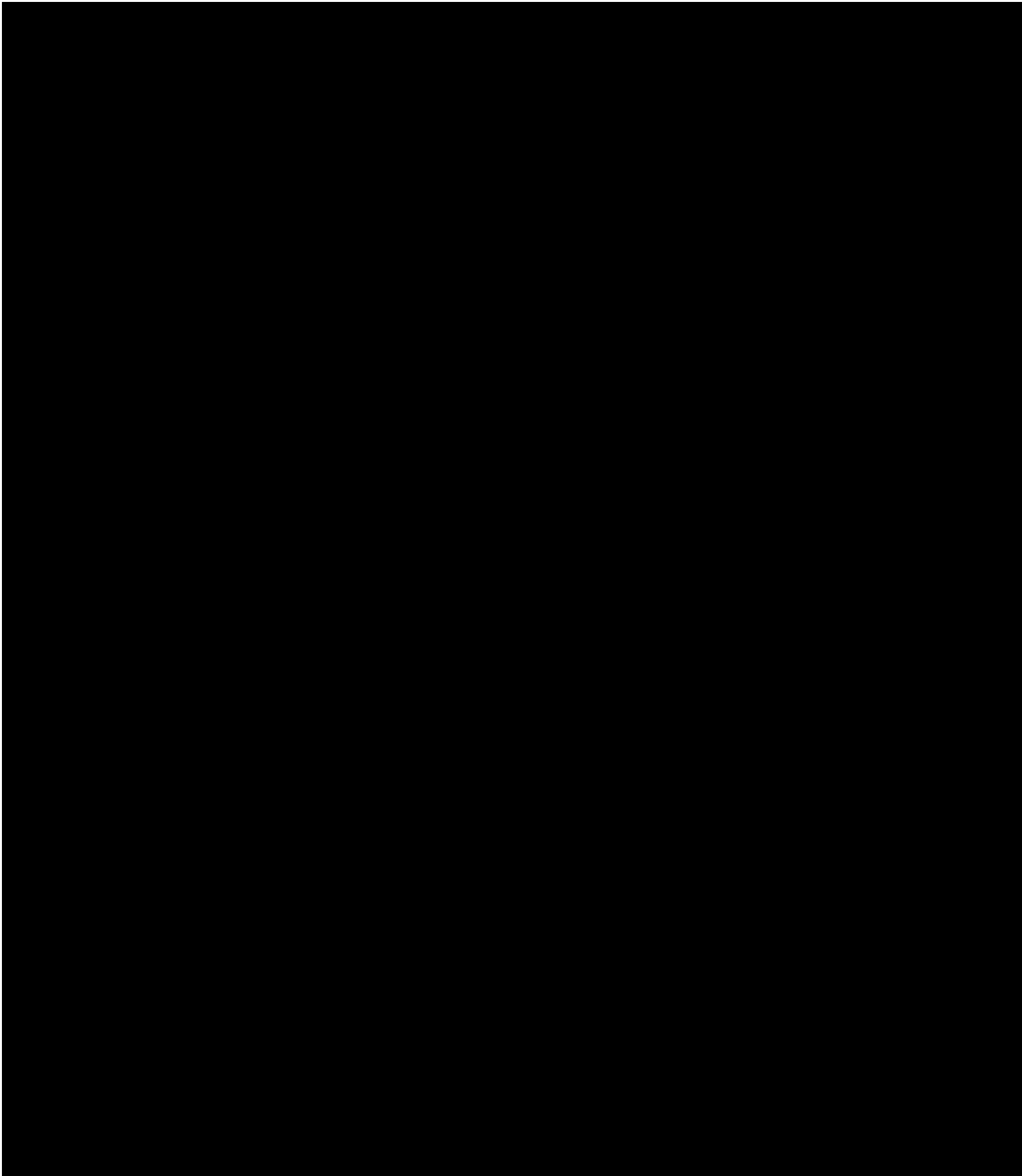


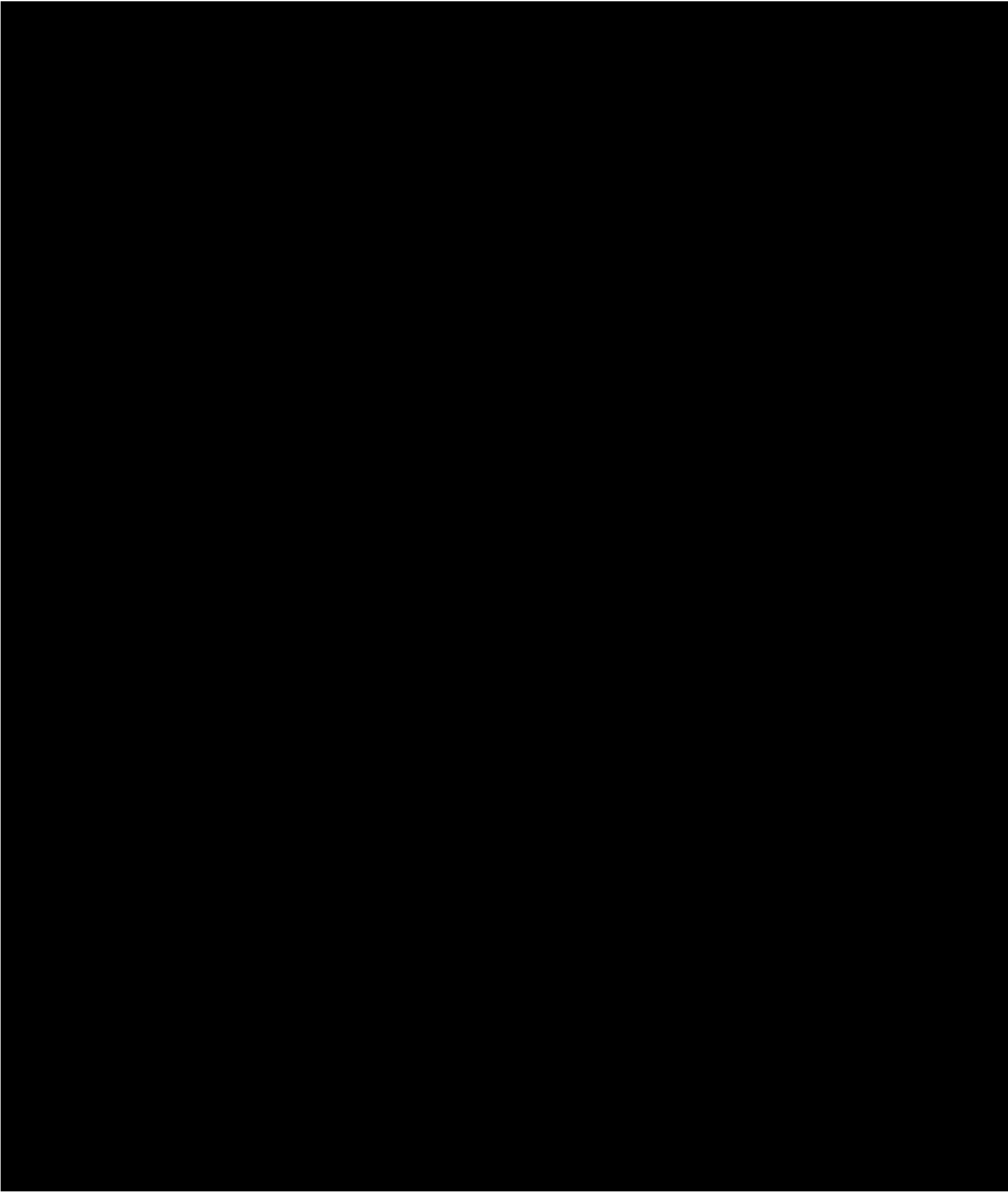












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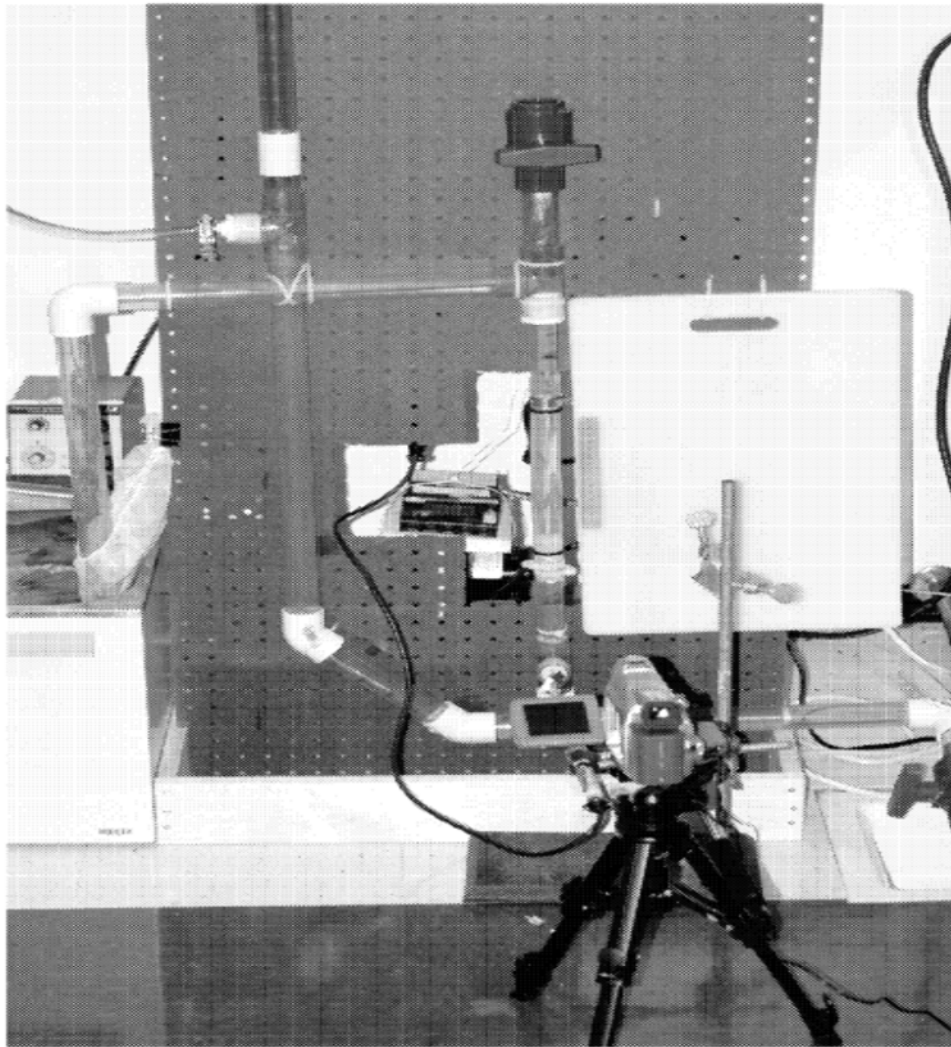
378. [REDACTED]

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<sup>485</sup> BPVE-01-00535555

Filter Migration Flow Loop Test Fixture



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**b. ETR-04-03-05 [GFO vs NMT] RNF Migration Resistance**

380. Engineering Test Report ETR-04-03-05 described the result of comparison of GFO-manufactured RNF filters to NMT (historical data only) for Migration Resistance, with the data from three test runs averaged.<sup>487</sup> The INTRODUCTION/BACKGROUND INFORMATION has as with TPR-04-02-02 that “Recent field activities indicate that migration failures have been reported for the RF product. Therefore, further testing of this specific characteristic is warranted.” The report continued to indicate that in conjunction with field activities and a special design review held on December 5, 2003 “to gain further understanding of the design elements of this product.” Both ETR-04-03-05 and TPR-04-02-02 have a discussion of the December 5, 2003 special Design Meeting and testing of migration resistance as a “critical element” for the DFMEA:

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<sup>486</sup> BPVE-01-00535555

<sup>487</sup> ETR-04-03-05 BPV-17-01-00153717

*In preparation for the special Design Review, the DFMEA for RNF was analyzed for critical elements...Migration resistance was one of the critical elements identified in the review. The outcome from this special Design Review was a list of action items, many of which related to migration resistance...Those migration resistant action items are being e addressed in this study.*<sup>488</sup>

381. ETR 04-03-05 tested a total of ten (10) GFO manufactured RF samples for each tubing size diameter (15 mm (RF11-RF-20, Lot 07KN2852-10 filters) and 28mm RF39-RF47 Lot 07KN2866 (9 filters); 28mm RF58 (Lot 07KN2865) (1 filter)) were evaluated as part of the study. That head-to-head migration resistance information was not included ETR-04-03-05 by Bard's Engineering staff.
382. Five filters per run were tested three times by NMT (using historical data) and Bard's Engineering tested 10 GFO filters three times. Bard was attempting to re-create NMT's original 28mm simulated IVC migration test apparatus. There was no comparative testing of the SNF. Reportedly, Bard found no statistical differences and concluded that GFO filters and NMT (historical data) fulfilled the '50mm HG Migration Resistance' acceptance specification. However, there is a note that the sample populations tested using the 15mm diameter simulated IVC (smaller IVC model) were not statistically compared since the "NMT and GFO fixtures had different maximum pressures that could be attained which distorted the data."<sup>489</sup>
383. Because of difficulties encountered by Bard when it ran the 15 mm IVC test system made using NMT's testing set-up, the test apparatus was modified by Bard's Engineers to facilitate its conductance of 28mm IVC simulation testing. Despite the changes made to the testing system by Bard and the changes in the protocol—feeding in only one clot at a time—the Engineering Report describes no direct head-to-head comparison of remaining stock of NMT filters to production GFO filters or production GFO filters to production SNF as a process 'control' using the same modified test apparatus. The migration resistance of SNF should be known and could have been used to address the effects of Bard's system and protocol modifications.
384. Bard learned that the non-calibrated Harvard transducer it obtained from NMT and used for testing did not operating correctly. According to Bard, NMT indicated that its protocol had NMT check the function of the transducer each test run to verify the transducer was in proper calibration and working. According to Bard, based on NMT's statement, it was "safe to assume that the unit went out of calibration sometime after NMT's testing."<sup>490</sup>
385. In terms of Quality Assurance, there was no discussion that Bard's results for GFO filters tended to show greater variation (standard deviation) than NMT's historical data. There is no discussion by Bard that 10% of its GFO filters tested 'failed' to perform as intended and the data was eliminated (dropped) from the 28mm IVC test data. The differences in the testing systems between Bard and NMT are most evident looking at the discounted Bard 15mm IVC simulation.

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<sup>488</sup> ETR-04-03-05 BPV-17-01-00153717; TPR-04-02-02 BPVE-01-00535555

<sup>489</sup> ETR-04-03-05 BPV-17-01-00153717

<sup>490</sup> ETR-04-03-05 BPV-17-01-00153717

This test attempt to use NMT's original test apparatus and protocol. The variation in the outcome data should have raised questions to Bard QA about reproducibility and comparability of data (validity of the testing) between the two testing facilities (Bard vs NMT) conducted at two different times and with two different protocols and two different testing fixtures. Bard wrote that "due to the low height of NMT's lab ceiling, pressure values peaked between 64mmHG and 100mmHG. Higher values were able to be obtained at BPV by removing ceiling tiles."<sup>491</sup> Again the two 28mm IVC simulation systems are being run at different sites, conditions and pressures when even the height of the ceiling at the testing facility can impact the comparability of testing data. Bard also wrote that "Note: Due to silicone tube bursting at a high pressure for the 15mm GFO Recovery Filter testing, testing was stopped at pressures that reached 3psi (155mmHG) for runs that followed." Reaching such high pressures for migration resistance for a GFO filter compared to a NMT results (using NMT's description of its testing apparatus and procedure) should have raised questions to Bard's Engineers regarding the accuracy and direct comparability of the filter performance. Bard's engineers added a thermocouple and temperature display to improve the temperature control of the system. The Bard fixture had the PVP piping reamed to smooth the edges and prevent clots from getting caught on the rough transitions in the PVC piping.

386. In addition to Bard's changes in the test apparatus, it changed the surface of the test and the site of attachment of the filter. For the sausage casing lining the silastic tube, Bard inverted it upon itself to create two layers of casing (not one layer as used by NMT to simulate the wall of the IVC in the tube). The fold of the casing was then positioned on the bottom of the simulated IVC where the casing could be attached to the tube via PVC piping. Bard used three transducers (not one used by NMT) to ensure there were two-calibrated transducers and one-non-calibrated transducers to ensure similar reading. The data summarized in the report would be obtained from only one of the transducers (not an average of pressure readings).

387. NMT, unlike Bard, successfully had performed RNF migration testing using a 15mm IVC simulation, with a standard deviation of 6.0mmHG (range: 64-80mmHG). Bard, using the original version of the NMT test apparatus and protocol, identified it as "flawed" and not behaving as anticipated. Bard's testing produced a standard deviation of 19.37mmHG (range: 110.2- 202.2mmHG). Therefore, either the two systems were different or the RNF were different or both since they did not provide similar and comparable results.

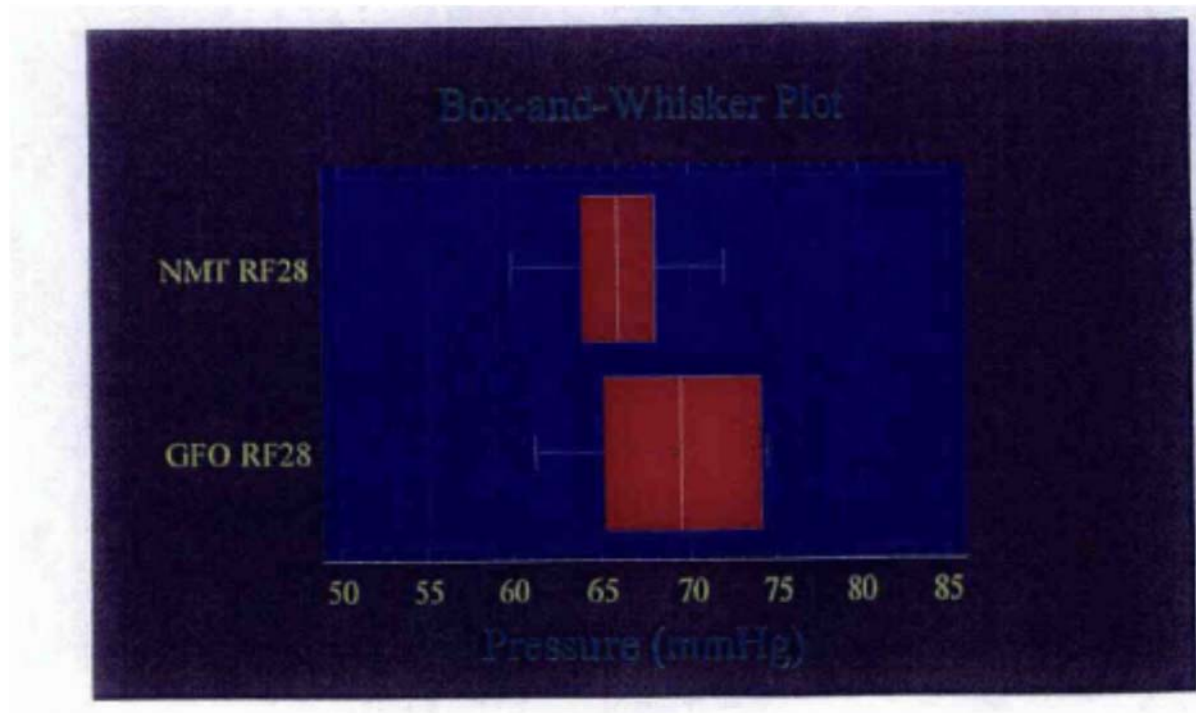
388. Bard did not provide a method to ensure control or comparability of data and outcome. One method would have been the use of the SNF which has known values for both NMT. Bard also had SNF values from TPR-04-02-02.<sup>492</sup>

389. For the 28 mm IVC simulation, there is following Box-Whisker Plot for GFO filters and NMT Historical filter data:

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<sup>491</sup> ETR-04-03-05 BPV-17-01-00153717

<sup>492</sup> ETR-04-03-05 BPV-17-01-00153717



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390. Slightly later in the report is a Table of Test Results (Bard Table 1):

Table 1: Migration Test Results						
Description	Filter Sample Size (n)	Total Run Quantity (N)	Mean (mmHg)	Stand.Dev. (mmHg)	Min. (mmHg)	Max. (mmHg)
NMT Recovery Filters in 15mm Diameter	5	15	69	6.0	64	80
GFO Recovery Filters in 15mm Diameter	10	30	151.3	19.37	110.2	202.2
NMT Recovery Filters in 28mm Diameter	5	15	66	6.8	57	76
GFO Recovery Filters in 28mm Diameter	10	26*	69.2	6.70	55.9	83.1

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However, when the 28mm IVC simulation data is placed together into a single table comparing the Whisker-Plot data to Bard Table 1 results, which did not occur in the report, there is a discrepancy in the data generated. The discrepancy is greatest for Bard's GFO filters, being tested on the modified Bard apparatus which is not addressed in Bard's Engineering Report.

28mmIVC	Source	Mean	Stand Dev	Min	Max
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<sup>493</sup> ETR-04-03-05 BPV-17-01-00153717

<sup>494</sup> ETR-04-03-05 BPV-17-01-00153717

Whisker	GFO	69	5.0	61	75
Table 1	GFO	69.2	6.70	<b>55.9</b>	<b>83.1</b>
Whisker	NMT	66	2.0	60	74
Table 1	NMT	66	6.8	57	76

391. Four of Bard's Recovery GFO filter 28mm IVC simulation (4/30 = 13%) were eliminated from the data with two samples (7%) called ineffective at stopping the simulated clots. Another GFO filter had the hooks unable to engage (i.e. anchor) in the sausage casing (simulated vessel wall). Bard's GFO did not obtain new filters for testing to ensure a sample size of 30 filters. However, as not address by Bard's Engineering Report regarding migration testing, of the 30 filters tested made at GFO in a 28mm IVC simulation model, there was a demonstrated failure of a Recovery filter to anchor or stop clots in 3/30 = 10%. This should have been a significant number of failed RNF filters during bench testing in terms of triggering a filter review for QA/QC. Bard identified the failures in the GFO testing:

Four 28mm simulated IVC runs were not applicable due to the followings reasons:

- o The filter never migrated and a pressure increase was unable to be obtained since the filter arm lifted up allowing clots to go past the filter. This occurred on 2 samples (RF40, run#2 and RF42, run #1).
- o The test was aborted by the technician since the sausage casing fold was incorrectly positioned on the top instead of on the bottom where it was to be clamped to the PVC piping. This occurred on 1 sample (RF40, run #3).
- o The filter hooks were not engaged in both layers of sausage casing. This occurred on 1 sample (RF41, run#1).

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392. The discarded values obtained by Bard for the GFO 15mm IVC simulation do not appear to correlate to the results of the NMT's historical 15mm IVC simulation testing.<sup>496</sup> The 15mm IVC simulation was reportedly the original testing fixture and procedure used by NMT. There is no real explanation as to the effects Bard's alterations had on the testing system and procedure for 28 mm IVC simulation testing compared to NMT. This makes it even more important to include the predicate SNF to look at migration resistance on the same testing apparatus versus historical data. The changes in the testing method without the use of known controls such as the NMT RNF or SNF cast doubt on the overall reliability of the data. Based on the testing, the GFO devices fulfilled the 50mmHg release specification as used by NMT but it has not clinical significance without the SNF data as to the acceptability as a permanent implant.

### c. Starguide Filter Migration Testing

393. On March 24, 2004, during an investigation to look at product from an alternative Nitinol supplier for Bard production in terms of qualification of material for a company named Starguide,

<sup>495</sup> ETR-04-03-05 BPV-17-01-00153717

<sup>496</sup> BPV-17-01-00153717

called the “Starguide Filter Migration Test Results” identified secondarily that the current commercial RNF product was failing to meet the critical 50mmHg migration resistance specification referenced in the cleared 510(k) for commercial release.<sup>497</sup>

394. Bard stumbled on to a major quality assurance and regulatory problem. The RNF did not even meet the 50mmHG release specification. Bard’s RNF released from GFO prior to March 2004 were all potentially outside specification for migration resistance, not consistent with the product cleared in the 510(k) and defective (violative).
395. According to an internal email of March 24, 2004 sent to Charlie Benware and Ed Fitzpatrick, with copy to Brain Hudson and Rob Carr, Subject: “*Starguide Filter Migration Test Results*,” Bard was testing the performance of RNF Filters made from a new Nitinol metal supplier, Starguide, to ensure the new filters material met the 50mm Hg migration resistance specification. A total of 40 filters were made and tested, each three times for a total of 120 runs. A quantity of 10 filters from each of the three lots were tested (n=30 Starguide Nitinol wire). A quantity of 10 filters manufactured using the current wire supplier were also tested for comparison (current manufacture RNF Filters).<sup>498</sup>
396. There were values below the 50mm Hg acceptance criteria for all three Starguide manufactured lots. Bard then tested migration resistance of the manufactured filters with the current supplier wire to see if the issue was the wire of the testing method. Values were identified below the 50mmHg migration resistance acceptance level with the current production lots. This pointed to a possible manufacturing issue with the “migration resistance testing” procedure.<sup>499</sup>
397. When GFO had previously done the migration resistance testing and compared it to the historic NMT data, all data values were above the minimum 50mmHG and found acceptable.<sup>500</sup>
398. At the time of GFO’s testing a new batch of “sausage casing” had been purchased to complete the testing. Operators at that time noted no differences between the behavior of the prior sausage casing and the new casing. Both casings came from the same supplier.<sup>501</sup>
399. In any case, Mr. Tessmer concluded that more testing will be necessary since the Starguide Nitinol wire “should be approved.” So, in March 2004, Bard learned its production filters were failing to meet the specification of 50mmHg migration resistance. Bard did not identify a cause and corrective action and it did not remove the defective filter lots shown to failing the minimum 50mmHg. Bard also did not quarantine the defective so they would not be released to implant in patients. Bard took no remedial action to identify when the commercial product had begun to fail the minimum migration release criteria.

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<sup>497</sup> BPVE-01-00330122. Tessmer Exhibit 9

<sup>498</sup> Tessmer Exhibit 9

<sup>499</sup> *Id.*

<sup>500</sup> *Id.*

<sup>501</sup> Tessmer Exhibit 9

**d. Competitive filter comparison.**

400. Bard approved a communication to be given to the Interventional Sales force to reaffirm that the RNF is “roughly equivalent” and “performs as well as competitors.”<sup>502</sup> There is a February 25, 2004 Filter Migration Test Results – Competitive Comparisons Migration “Special Design Review” which shows the RNF with substantially lower resistance to migration in simulated vena cava than competitors and the SNF.<sup>503</sup> The RNF failed to meet the 50 mm Hg specification that is listed in the 510(k) given to FDA.<sup>504</sup> The RNF is therefore not substantially equivalent to the predicate SNF and not consistent with the cleared 510(k).
401. In terms of marketing of the RNF, physicians had been reporting that the RNF has “tilted quite a bit” when they went to retrieve them.<sup>505</sup> Therefore, on February 26, 2004 Janet Hudnall recommends that Bard’s sales force and marketing cut back claims regarding “caval centering.” She told Marketing that with the changing experience for RNF, *“now that we have more experience with Recovery the positioning of ‘tilt-resistance should probably be downplayed.”*<sup>506</sup>
402. Bard’s Dr. Lehmann conducted a March 10, 2004 Health Hazard Evaluation (HHE)<sup>507</sup> “RE: Migration risk.” There is a second HHE on April 27, 2004 by Dr. Lehmann,<sup>508</sup> a third on June 30, 2004, (10 patients explanted), by Dr. Ciavarella<sup>509</sup>; another on July 9, 2004 for Migration with Dr. Ciavarella,<sup>510</sup> November 17, 2004, with Dr. Ciavarella RE: Limb fractures of RNF,<sup>511</sup>; and December 17, 2004 Dr. Ciavarella for 76 reported serious hazards.<sup>512</sup>
403. According to a HHE of June 30, 2004, migration of the RNF was classified by Dr. Ciavarella with the severity of “catastrophic.”<sup>513</sup>

**6. Bard’s Good Manufacturing Practices/Quality Systems (GMP/QS) and Internal Standard Operating Procedures (SOP) failed to stop it from selling an adulterated and misbranded product.**

404. As part of FDA’s required Good Manufacturing Practices of Quality Systems Regulations (QS) and Bard’s internal SOPs designed to implement the QS (21 CFR § 820), Bard was required to adequately investigate complaints and reports of patient injuries and death. Bard was also

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<sup>502</sup> BPV-17-01-00164702

<sup>503</sup> BPVE-01-00410985

<sup>504</sup> BPVE-01-00410985

<sup>505</sup> BPVE-01-00373887

<sup>506</sup> Hudnall Exhibit 24; BPVE-01-00373887

<sup>507</sup> HHE-modeled after 21 CFR part 7 and the action of the FDA to classify health hazard risk for the public with FDA regulated products; BPVE-01-00510989

<sup>508</sup> BPVEFILTER-01-00043728

<sup>509</sup> BPVEFILTER-01-00014836

<sup>510</sup> BPVE-01-000245369; BPV-DEP-00004730

<sup>511</sup> BPVE-01-00103875

<sup>512</sup> BPVE-01-01019821

<sup>513</sup> BPV-17-01-00024667

required to identify the cause of device failures, including reports of fracture, perforation, migration, embolization, patient bleeding and injury, additional surgeries associated with the filters including removal and reports of patient sudden deaths. Bard's SOP should have been sufficient to establish Bard's methods for implementation of effective failure investigations, corrective and preventive action, notification of physicians and FDA, conduct a recall in order for Bard to return itself back to full compliance with the Act. Bard also had the ability to switch marketing for a permanent IVC filter back to SNF.

**a. Redesign of RNF**

405. The first Limited Market Release of the GFO RNF product was in April 2003. The retrieval option was cleared July 2003 with the first report of a migrated limb fracture December 2003. By April 2004 Bard HAD already begun a "Redesign of Recovery." As of June 2004, Bard was aware of risks of RNF, that it was not meeting its own minimum acceptance criteria and continued to leave the RNF, Bard's only cleared retrievable filter, on the market. It would continue to leave the RNF on the market without any notification of physicians or FDA despite silently stopping production in September 2005 without recall of RNF stock remaining on shelves.

**b. Distensibility Testing**

406. When John McDermott, Bard Peripheral Vascular President, sent an email to Len DeCant on July 26, 2004 Bard's VP of Research & Development, he instructed Mr. DeCant to "*make sure we are doing some kind of testing to determine the distensibility of the cavas.*"<sup>514</sup> Mr. Uelmen was asked based on that July 2004 email if at some point Bard became aware that the vena cava could distend by 25 to 50% and his response was "Yes."<sup>515</sup> Based on the email, when asked if Bard had not incorporated bench testing for distensibility of the simulated vena cava in July 2004 at time of the email, Mr. Uelmen replied "Yes."<sup>516</sup>

407. Mr. DeCant responded to Mr. McDermott's July 26, 2004, email with a cc to Rob Carr:

*It is unclear on the expected action. To date we have conversations with clinicians and reviews of scientific journals. We know that it distends and we suspect that it distends considerably by 25-50%. Rob and I have discussed repeating the distensibility work we have done in the past on pigs. We have also talked about potentially adding a distensible tube in the migration resistance test but this is unproven that it would work at this time. Is this the type of testing you had in mind?*<sup>517</sup>

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<sup>514</sup> Uelmen Exhibit 6; BPVE-01-00009626

<sup>515</sup> Uelmen depo Vol I p 157, l. 5-23

<sup>516</sup> Uelmen depo Vol I p 160, l. 12-22

<sup>517</sup> Uelmen Exhibit 6; BPVE-01-00009626

408. Mr. McDermott replied that he didn't know what type of testing should be done but he thought it was important for a device design that anchor on the vessel wall:

*I don't know what the test should be (animals, humans, bench, etc.), but I think we should try to better quantify and understand how much these vessels expand if we're designing a device to anchor on/in the wall. Do you feel that we already have a handle on this dynamic?*<sup>518</sup>

409. Mr. DeCant's response:

*A good as anybody. I think the real question is how to incorporate distensibility in our bench testing both in terms of methodology and acceptance criteria.*<sup>519</sup>

410. Ms. Raji-Kubba replaced Mr. DeCant at Bard as VP of R&D from May 2007 through December 2011. She was asked how Bard learned about the vena cava. She said that they spoke with clinicians, scientists, engineers to get a better grasp of the vena cava functions. However, she could not recall any names of experts or literature specifically consulted with regards to researching the vena cava.<sup>520</sup>

411. Mr. Uelmen, testified that he was aware of Dr. Asch's study and he was aware of the fractured filter leg occurring in the pregnant patient. He did not remember that a filter had migrated in the study.<sup>521</sup>

412. Mr. Uelmen was shown a "Bard Peripheral Vascular Filter Franchise Review" dated May 6, 2008, a period after he left Bard. The presentation continued to support that in 2008 Bard, despite Bard's active marketing and sales of IVC filters for off-label and unapproved uses, it was aware internally that Bard still had a 'lack of understanding of the caval anatomy that impacted its test methods' and lack of understanding of user needs (physician and patient) with its implanted IVC filters for prevention of PE was a "Weakness" for "Increasing Revenue and Capturing more market share":

***SWOT: Objective: Increase Revenue and Capture More Market Share***

***Weaknesses:***

...

*-lack of thorough understanding of the dynamics of the caval anatomy-impacting testing methods*

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<sup>518</sup> *Id.*

<sup>519</sup> *Id.*

<sup>520</sup> Raji-Kubba deposition 7/18/16, p. 30-34, L.2-2

<sup>521</sup> Uelmen depo Vol I p 162, l. 3-19

*-We have historical reactive/evolution design mindset*

*-Product complications-forcing focus on reactive designing??*

*Limited understanding of user needs*<sup>522</sup>

413. In an internal email series starting on February 27, 2004 between Janet Hudnall and David Rauch discussing a sales training piece he had created, Subject: "Case for Caval Centering,"<sup>523</sup> Ms. Hudnall wrote regarding the focus of the marketing message on the ability of the Recovery Filter to remain centered in the cava. According to her comments filter centering was not what physicians were reporting back to Bard for the Recovery Filter. Her email also supports the lack of knowledge about the performance of the Recovery filter following its 2003 launch. Ms. Hudnall wrote to Mr. Rauch (underlining added for emphasis):

*I wanted to comment on the training piece you created...*

*I must strongly caution against emphasizing Recovery's ability to center in the cava to the point where it is the focus of the product's positioning. We knew very little about the long-term clinical performance of that device when we launched it. After a year of commercialization, there are still many questions that need to be answered. One thing that we do know, however, is that Recovery does not always stay centered in the cava. In fact, physicians will often find that it is tilted quite a bit when they go to retrieve it even though it seemed perfectly centered upon deployment. So, it seems to be that selling the device solely on this feature could set the sales rep up for some uncomfortable situations in the long run.*<sup>524</sup>

414. David Rauch's response back to Ms. Hudnall on February 27, 2004 also emphasized Bard's changing experience with the performance of its Recovery Filter and making alterations to its marketing emphasis:

*You are right; now that we have more experience with Recovery the positioning of tilt-resistant should probably be down played...*<sup>525</sup>

**B. 2004 Bard hired a third-party auditor to look at filter manufacturing and QS history.**

415. Only fifteen months after release of the Recovery filter, Bard hired a third-party auditor, Quality Systems Engineering, Inc. to look at its IVC filter manufacturing practices. This followed after Bard's receipt of more reports of Recovery migration and patient deaths. At the time of the audit, Bard was already engaged in development of its next generation G2 (Generation 2) Filter. The QSE auditor verified the prior flawed history of Bard's development and design of the Recovery

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<sup>522</sup> Uelmen Exhibit 7

<sup>523</sup> BPVE-01-00373887

<sup>524</sup> Carr Exhibit 3

<sup>525</sup> Hudnall Exhibit 24; BPVE-01-00373887

Filter and contribution to the problems reported for the device. A major Bard flaw had been its total reliance on NMT's design and development. Bard had accepted and produced a Recovery filter it received from NMT. There were gaps created by Bard's lack of rigor to review NMT's device design process. As was being supported by Mr. Hudson's QA memorandum in December 2003 (see above), Bard had not performed its own due diligence, testing and validation to ensure the adequacy and risk of NMT's filter design.<sup>526</sup>

416. According to QSE's findings, Bard's Design Input and Design Validation had fallen short for a medical device manufacturer in respect to investigation of risks for migration and potential causes. For example, Bard failed to have appreciated with Recovery's design that the patient's IVC could distend after filter placement. As a result, Bard had failed to conduct testing that would appropriately simulate how the Recovery Filter would perform when implanted.
417. As noted in Bard's revised DFMEA for Recovery, there had been no testing in place to control for changes of patient vena caval distention.<sup>527</sup> Thus, according to the findings of the QSE auditor, Bard discovered its device was failing and causing patient deaths from a failure mode or phenomenon that it had not originally realized could occur and for which there were no safety tests in place to evaluate or control the risk.
418. In June 2004, Bard convened a multidisciplinary panel of physicians to discuss IVC filter complications. With regard to filter migration the panel's perspective was different than Bard's. The panel members indicated that filter migration should occur less than 1% of the time. For prophylactic filter placement, migration to the heart should virtually never happen. The rate of occurrence of migration should be less than 1 in 1,000.

*○ Migration should not be different for retrievable filters than for permanent filters.*

*○ A retrievable filter is expected to perform just as well as a permanent filter*

*○ A filter should not migrate; no matter what size of thrombus burden it capture.<sup>528</sup>*

419. In a PowerPoint presentation intended for Bard Management Review in May 19, 2006 (with data current to May 18, 2006) there was a slide titled 'Recovery Chronology' that showed the discontinuation (but not the recall or market retrieval or physician/FDA notification) of the Recovery in September 2005, with the first detached limb (fracture) complaint received in December 2003.<sup>529</sup>

<sup>526</sup> BPV-17-01-00101710; BPVE-01-00031037

<sup>527</sup> See 1999 Guidance

<sup>528</sup> BPVE-01-00617777

<sup>529</sup> BPVE-01-01511339; Schulz Exhibit 15

420. The Bard Management Review also included a slide that clearly showed that Bard knew about the differences between the SNF (predicate), a filter which it sold in the United States since the 1990s, and the risks of RNF in terms of reporting rate of fractures (.30% vs 0.01%).<sup>530</sup>
421. The bulk of the 102 analyzed fractured RNFs were detected at time of filter retrieval (68%). The other 33 returned to Bard were identified at time of imaging (10, 19%), as a result of treatment of a patient's symptom of pain (i.e. during surgery) (13, 13%), following a death and at autopsy (1, 1%), and 9 the time of identification of the fracture was unknown (9, 9%).<sup>531</sup>
422. The greatest number of 102 returned RNF fractures for analyses were received from women – 53/102= 52%. However, removing the unknown 40 filters, females accounted for 53/62 returned fractures= 85% with the majority classified by Bard as 'asymptomatic'.
423. Bard looked at the differences in age and gender in terms of the recovery implant population. For females with known age (N=40), there was a greater distribution in ages female range: [15yrs (pediatric)-87yrs (geriatric) ] than males with known age (n=6) males: [18 years to 48 (adults)] in the returned filters.<sup>532</sup>
424. Only 1 returned male filter had weight reported= 190 lbs. For the females with returned fractured filters with weight information (N=17), the female weights ranged [<100 lbs to >500 lbs] with 10 fractured filters (59%) in female patients < 150 lbs. So the returned 'fractured' RNF filters were occurring in relatively smaller women (<150lbs).<sup>533</sup>
425. Bard also looked at the IVC size information provided for the returned fractured RNF filters available for N=7 of the female patients (and N=4 for unknown gender). The IVC size ranged from (11mm to >28mm). By the table for Age, there was implantation in a female pediatric patient (15 years) with a filter fracture. Four of the women (57%) had filter fracture with an IVC < than 28 mm IVC. No woman or 'unknown' gender of the total 11 returned fractured RNF had an IVC recorded as equal to 28mm. Three women (N=7) had an IVC > 28mm (43%). Women by this analysis were prone to filter fractures with IVCs either < 28mm>, with the only one identified 'symptomatic' patient, a female with an IVC <20mm. For 5 of the 7 female patients (71%), it was 'unknown' if the patient was asymptomatic or symptomatic. The trend was showing that the risk of filter fractures by this analyses occurred in IVCs not 28mm and fractures could be symptomatic with RNF in smaller IVCs.<sup>534</sup>

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<sup>530</sup> BPVE-01-01511339; Schulz Exhibit 15

<sup>531</sup> BPVE-01-01511339; Schulz Exhibit 15

<sup>532</sup> BPVE-01-01511339; Schulz Exhibit 15

<sup>533</sup> BPVE-01-01511339; Schulz Exhibit 15

<sup>534</sup> BPVE-01-01511339; Schulz Exhibit 15

426. Bard also looked at the time until discovery of the RNF fracture. It identified that fractures could be discovered “late” at 700 days as RNF ages, both symptomatic and asymptomatic. This should have supported Bard’s duty to notify physicians to continue to monitor patients for late filter fractures as the filters remain implanted in patients and age. The data also does not support that RNF is substantially equivalent as a permanent filter as the SNF predicate as claimed to FDA for marketing.
427. Bard’s analysis showed that for the RNF, the most common site of filter detachments (fractures) based on 132 filter fractures was the RNF’s Arm (91/132=69%). For 76 patients of N=102 returned fractures for analysis (75%), 129 pieces/fragments/fractured filters continue to remain implanted in those 76 patients ( 26 with fractured filters and 69 fractured arms).<sup>535</sup>
428. Bard also looked at the fracture analyses of RNF in terms of a received complaint description. The greatest number of fractures were associated with a reporting of filter “tilt.” RNF with fractures had greater reporting of cephalad migration (N=4) compared to caudal (N=2). Fracture and tilt N=15 had 9 filters (60%) removed compared to 6 filters (40%) left remaining. Fracture and saluting arm N=9, of the 7 with information, 4 filters removed (57%) compared to 3 filters (43%) remaining, there was loss of information for 2. Nine filters had reports of “perforation/penetrate.”

**C. 2004 Bard hired Altran Corporation to conduct a failure analysis of returned RNF with fractures.**

429. Bard sent 11 filter samples to Altran Corporation to conduct a failure analysis for returned filters. Bard wanted Altran to identify a common failure mode for the specimens. There is a draft September 20, 2004 report titled “Failure Analysis of Eleven Complaint Vena Cava Filters Technical Report 11-0245-00-TR-01, Revision 0.”<sup>536</sup> The report was prepared by Altran for CR Bard-Glens Falls Manufacturing.<sup>537</sup>
430. Specimens were received with identified failures of: hook (4), arms (3), leg (1), arm/hook (3). The most common RNF failure occurred in the hook. The fewest reports were for a failure of the leg. On scanning electron microscopy (SEM) damage was seen produced by wire corrosion or rubbing contact. The pattern of failure for the arm’s wire was identical to the failure for other wires examined. For all the filter wires with fractures, a fracture initiated at the inner edge of the wire and propagated towards the outer edge resulting in a final ductile overload fracture.<sup>538</sup>
431. The results of the SEM evaluation of the failed filter arms, hooks and legs indicated all failed in a similar manner. The presence of a “thumbnail” pattern on the fracture surfaces showed that the wires experience initial cracking either prior to or during service (implanted). The initiation areas

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<sup>535</sup> BPVE-01-01511339; Schulz Exhibit 15

<sup>536</sup> BPV-17-01-00086376

<sup>537</sup> BPV-17-01-00086376

<sup>538</sup> BPV-17-01-00086376

of some of the fractures surfaces show possible damage due to corrosion or rubbing of the mating surfaces. The damage also indicated that these initial cracks had existed in the metal for some time prior to final failure. In all cases the final fracture occurred when the crack reached a critical size in the overload failure.<sup>539</sup>

*As seen in the results, most but not all fractures began on the inner side (the side facing toward the center of the filter) of the arm wires. The cause of the variation in the locations of the initiation points of the arm, hook and leg wires is not understood.*<sup>540</sup>

432. Altran suggested that a stress analysis and a root cause investigation would provide additional insight into the cause of the wire failures.<sup>541</sup>

433. The examination of the Nitinol wire fractures by SEM by Altran indicated ongoing changes in the wire consistent with filter aging as well as corrosion and rubbing. Therefore, as the filter wire age, there will be greater fatigue and increased risk for fracture development.

434. Based on the analysis of Altran, the following is provided as background on the metal used and concerns of Bard in 2004. Cindi Walcott sent an email to Rob Carr on July 7, 2004, prior to the circulation of the Draft Altran report. Her email was "Subject RE: Dr. Ciavarella's Recovery Filter Questions," and Mr. Carr responded:

***Q. Has there been any bench testing regarding the recovery Filter detached limbs, similar to the type done for migration?***

*A. We have begun to develop a test method that will simulate the fracture environment that we believe the filter is in. To date, we do not have a good test that has given us our expected results.*

***Q. Has there been comparative fatigue testing done since with regards to competitive filters?***

*A. We have not compared the Recovery against other filters. In the development process, we did standard fatigue testing to ensure that the filter would not fracture.*

***Q. Is there a variation in the metal used with regards to the competitive filters?***

*A. Yes. The Recovery and Simon Nitinol filters are made of Nitinol wire, the TrapEase and OptEase filters are made of Nitinol tubing. The Tulip is made from Eligoy, the Greenfield is made of either stainless steel or titanium, and the Vena Tech LP is made of Phynox*

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<sup>539</sup> BPV-17-01-00086376

<sup>540</sup> BPV-17-01-00086376

<sup>541</sup> BPV-17-01-00086376

***Q. Could the detached limbs have some sort of correspondence to any deployment issues or tilting issues?***

*A. Because we have not been able to point to a specific root cause, we are unable to answer this question definitely. Our assumption is that the arm that fractures is inverted upward and has not been associated with implantation*

***Q. Could the detached limbs have some sort of correspondence to any structural features on the Recovery Filter?***

*A. We believe that we can improve the fracture rate of the filter arm by changing the sharp angle of the arm of the current design to a softer radiused arm (not proven). For the hooks, we believe that the issue is more related to surface treatment (centerless grinding) and is a different mechanism.<sup>542</sup>*

#### **D. Bard's development of a Remedial Action Plan for RNF.**

435. Bard's Recovery Filter Migration Remedial Action Plan (SPA-04-04-02) of April 21, 2004, was reviewed by Bard's Corporate Product Assessment Team (PAT) Reviewers, with sign-off by Peter Palermo, VP, QS.<sup>543</sup> It was made following Bard's receipt of report of the second patient's migration death associated with the RNF. The report came directly from a medical examiner, Dr. Banner, on April 14, 2004. Bard's Department of Risk and Compliance were notified by the medical examiner of the patient's death. The medical examiner attributed the patient's death to Bard's IVC filter (complaint Report #5922). On April 19, 2004, members of Bard's Division PAT met with Dr. Banner and the hospital to obtain additional information about the patient's death.

*The team met again on April 21, 2004 to discuss all information obtained in order to bring resolution to this issue.<sup>544</sup>*

436. Based on the information obtained for the second patient's death, the IVC filter had been properly implanted in the patient. The clot formation was called 'antemortem' with the thromboembolus measuring 3 cm by 5cm. As a result of Bard's investigation, it was concluded by Bard that there was no manufacturing or design defect associated with the patient death.<sup>545</sup>

437. The MedWatch report submitted from the hospital risk manager to the FDA indicated that the Recovery Filter had been placed approximately 13-days prior to the patient's death. The patient was not at the hospital at time of death.

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<sup>542</sup> BPV-17-01-00002142

<sup>543</sup> BPV-17-01-00153578

<sup>544</sup> BPV-17-01-00153578

<sup>545</sup> BPV-17-01-00153578

438. By April 2004, Bard tracked at least six instances reported to BPV's Field Assurance when an IVC filter had migrated [ $>2\text{cm}$ ]. The results provided to Bard from the migration:

*#1) Death from migration to the heart;*

*#2) Filter remains in place outcome not specified;*

*#3) Unsuccessful filter manipulation to try to reposition the filter and untwist the legs resulted in migration to the heart, outcome not specified;*

*#4) Surgery required when the patient became symptomatic (shortness of breath, lightheaded) to remove the filter;*

*# 5+#6) Two patients asymptomatic and filters removed.* <sup>546</sup>

439. This was now the second patient's death received by Bard associated with a migration of the Recovery Filter into a patient's heart. By April 2004, a total of 8,200 Recovery Filters had been distributed (number implanted not indicated).<sup>547</sup> Yet, Bard, in contrast to the history of the SNF, now was aware of at least two patient deaths associated with filter migration (embolization) to the heart.

440. In terms of Bard's QA investigation of the April 2004 patient's death report, the subject's filter production lot number was 07LN2037. The entire manufactured lot contained a total of 37 units.<sup>548</sup> The conclusions of Bard's PAT reverted back to Dr. Lehmann's email responding to the April 15, 2004 email (Subject: RE: "Crisis Communication Plan and Supporting Documents for Recovery Filter") to Bard's Lynch Lee, Holly Glass, Donna Passero, Janet Hudnall and Kellee Jones.<sup>549</sup> Dr. Lehmann wrote the theme was: "This is a simple story we should repeat again and again ==bottom-line: good filter, severe case, bad outcome, deep regret."<sup>550</sup>

441. Bard described the "severe case" report of the patient death ('bad outcome') and findings and the justification for Bard to take no additional action to remove the product from the field, notify physicians or protect patients. Bard will continue to review the FDA's MAUDE database with under-reporting (not its more accurate complaint files- as required by GMP/QS) to determine what information has been received by the FDA (and is visible to competitors) (under lining for emphasis):

*o The BPV Product assessment Team has concluded that the Recovery Filter captured a large embolic load with resulting increase in venous pressure that lead to inferior vena cava dilation greater than 28mm resulting in migration...comparing data prior to receiving 510(k) for the Recovery indication (April through July 2003) and post recovery*

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<sup>546</sup> BPV-17-01-00153578

<sup>547</sup> BPV-17-01-00153578

<sup>548</sup> BPV-17-01-00153578

<sup>549</sup> BPV-17-01-00165419

<sup>550</sup> BPV-17-01-00165419

*indication (August 2003 to present) we concluded that although migration issues occurred after August 2003, there was insufficient quantity of product in the market prior to August 2003 (826 units) to provide meaningful comparison.*

*○Migration resulting in patient death requires the Division PAT to convene immediately and initiate an investigation per R-002. If the cause of the event is an anticipated adverse event and the occurrence rate does not exceed accepted frequency, the product will continue to be marketed during the investigation. If at any time during the investigation, data shows the cause of the event to be unrelated to massive thromboemboli, the Division PAT shall immediately review all data gathered during the investigation and re-evaluate the status of the product as the investigation is completed per R-002 (massive thromboemboli)*

*○Vena Cava Filter Adverse Event frequency rates will be reviewed on a quarterly basis. Rates will be obtained from: MAUDE, IMS, Lexis/Nexis and other medical literature as identified during the search. A comparison of the Recovery Vena Cava Filter to all other Vena cava filters will be completed. Frequency rates will be compared to assure that adverse events associated with the Recovery Filter are not occurring with excess frequency- MAUDE: potential under-reporting, inadequate description of events in the MAUDE database result in potential misclassification; very low frequency of events, high variability in event rates and sales rates across devices and time periods; IMS, sales data can only be roughly estimated- potential over-reporting.*

*○Comparative adverse event rate will be tracked using MAUDE and IMD to assure that the adverse events associated with the Recovery Filter are not occurring with excess frequency.*

*○There has been no evidence design or manufacturing problem that was identified as contributing to the patient death associated with the Complaint Report*

*○The Division PAT was challenged to determine whether or not a filter without a recoverable indication could have resisted migration under the clot burden identified in this investigation.*

*○A review of MAUDE database shows that all Vena Cava Filters with the exception of SNF are subject to migration and are associated with deaths due to thromboemboli.*<sup>551</sup>

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<sup>551</sup> BPV-17-01-00153578

442. Bard's Paul Kowalczyk faxed a 56-page document to Mary Edwards dated May 11, 2004 regarding the "Recovery Filter Crisis Communications Plan."<sup>552</sup> In the documents, an email of May 10, 2004 had been sent from Lee Lynch and Kimberly Ocampo, Hill & Knowlton, to Bard's Holly Glass, Chris Ganser, Janet Hudnall, Donna Passero and Brian Berry. (Subject: Recovery Filter Crisis Communication Plan):

*This document provides a step-by-step guide for implementing an immediate communications strategy to ensure C.R. Bard is prepared for any news coverage that may result from pending investigations surrounding the Recovery Vena Cava Filter.*<sup>553</sup>

*As with previous crisis plans Hill & Knowlton has prepared for C.R. Bard, this guide will help Bard's Corporate Communications Team prepare for and properly manage controversial or negative stories surrounding the Recovery Vena Cava Filter.*

*The proliferation of unfavorable press in top-tier media outlets can cause an onslaught of negative activity; a company's morale may suffer, stock prices may plummet, analysts may downgrade the affected company's ratings and longstanding reputations may be ruined temporarily or even permanently.*<sup>554</sup>

**E. Bard's Dear Doctor letters did not provide adequate and accurate risk information to all physicians caring for patients implanted with the RNF.**

443. Despite Bard's sales force telling physicians that the RNF performed like other competitive IVC filters, based on Corporate's sales force communiqué and crisis management plans,<sup>555</sup> physicians based on the results of Bard's focus groups and surveys were not convinced. Bard's undated Dear Doctor Letter "IMPORTANT: INFORMATION FOR USE UPDATE"<sup>556</sup> developed as part of the 2004 Crisis Plan to response to patient deaths from migration was created as an "as needed basis."<sup>557</sup> It did not address the design and performance issues of the Recovery Filter based on Defendant's 18 months of clinical experience with the device. That is what the letter said it was intended to do for a physician, but that is not what it accomplished.

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<sup>552</sup> Edwards Exhibit 18

<sup>553</sup> Edwards Exhibit 18

<sup>554</sup> *Id.*

<sup>555</sup> BPV-17-01-00164702; BPV-17-01-00153578; BPVEFILTER-01-00043824; BPV-17-01-00097817; BPVE-01-00163350; BPVE-01-00268921, DeJohn Exhibit 348; BPVE-01-00033810; BPVE-01-00435296; BPVE-01-01019773; BPVE-01-00008821; BPVE-01-00167251; BPVE-01-00171311; BPV-DEP-00005665, Goodrow Exhibit 30; BPV-DEP-00004802, Friedman Exhibit 6; BPV-01-00299538;

<sup>556</sup> BPVE-01-00365312

<sup>557</sup> BPVE-01-00365312

444. Instead of telling the physician what was accurate, Bard blamed poor outcome of the RNF on the implanting physicians. Because of “physician error” it updated the instructions for use and was sending out the letter to learn about the IFU.<sup>558</sup>
445. In the second Dear Doctor letter of May 11, 2005, the poor performance of the RNF was once again not blamed on the filter’s development, design and testing by Bard as a permanent implant.<sup>559</sup> Bard did not address its marketing of an IVC filter for use in elective surgical populations without Bard providing surgeons adequate instructions for use and warnings. Bard did not provide the same safety information available in 1999<sup>560</sup> about the use of ventilation pressure changes, risk of distention of the inferior vena cava with a newly implanted filter. Now the adverse outcome was blamed on the morbidly obese bariatric patient. Instead of user error, the Recovery Filter failed because of the selection of the patient.
446. Despite what Bard knew in 1999<sup>561</sup>, the 2005 letter reinforced placing the filter in the 28mm IVC rather than accurately informing physician about NMT’s adoption of the < 24mm size recommendation for the IVC for the SNF. The letter also failed to inform physicians for a prophylactically placed filter in a surgical patients, when the vena cava <24mm, implant the device at least 2 weeks before the procedure to allow endothelial surface to form to help stabilize the implant. Surgeons and Interventional Radiologists were not informed that the use of general anesthesia and force positive pressure respiration can change the pressure gradients placed on the IVC including distension increasing the risk of migration.
447. The Dear Doctor letter failed to inform physicians that implantation of the Recovery Filter was not studied in morbidly obese patients for elective bariatric surgery. Physicians were not informed, as stated in the May 11, 2004, Recovery Filter Crisis Communication Plan, the first death report from RNF migration into the heart post operatively a male bariatric patient weighing 400-500 lbs.<sup>562</sup> His postoperative course was marked by prolonged intubation and Congestive Heart Failure (CHF). On day five he collapsed while sitting on the toilet and could not be resuscitated. The cause of death was attributed to circulatory collapse with thrombus-encased filter found in his right atrium. This information would be relevant safety information to physicians caring for bariatric patients. Bard did not send accurate information about the risks of the RNF family to all physicians and health care providers groups engaged in the care of implanted IVCF patients.

**F. Bard’s June 2004 physician focus group indicated Bard’s RNF was not performing as physicians expected.**

448. In June 2004, Bard convened a multidisciplinary panel of physicians to discuss IVC filter complications. With regard to filter migration the panel’s perspective was that it should occur

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<sup>558</sup> 21 CFR§ 1.21- Failure to reveal material facts

<sup>559</sup> BPVE-01-00429858

<sup>560</sup> Uelmen Exhibit 5

<sup>561</sup> Uelmen Exhibit 5

<sup>562</sup> Edwards Exhibit 18

less than 1% of the time. For prophylactic filter placement, migration to the heart should virtually never happen. The rate of occurrence of migration should be less than 1 in 1,000.

*○ Migration should not be different for retrievable filters than for permanent filters.*

*○ A retrievable filter is expected to perform just as well as a permanent filter*

*○ A filter should not migrate; no matter what size of thrombus burden it capture.<sup>563</sup>*

449. In a July 16, 2005, email to several Bard employees, District Sales Manager, Jason Greer suggested some selling points “[m]ay I suggest the safest filter on the market that has been on the market for the longest time in its current form...the Simon Nitinol Filter?” He continued, “If you want a filter that will give you the greatest chance of reducing your complications, the Simon Nitinol Filter is that filter (I have a spreadsheet from MAUDE that shows this).”<sup>564</sup>

**G. Bard stopped RNF distribution as September 2005 but did not conduct a recall or notify physicians of RNF risks for patients.**

450. Bard knew from its documents in 2004 that the RNF was not substantially equivalent to the SNF and the released product was not fulfilling the characteristics of device cleared for marketing by 510(k). It was aware of the differences when looking at the FDA’s MAUDE database and its own complaint database for the SNF and RNF. It was aware of differences when it held a Special Design Review in December 5, 2003. It was aware of the differences and the risks described in a series of six internal Health Risk Evaluations (HHE) conducted throughout the year 2004. The July 9, 2004 HHE for RNF Migration conducted by Dr. Ciavarella, the fourth HHE, which he sent to Mr. Uelman, VP of QA compared the fracture rate of the RNF to competitor IVCF and found that all other IVCF combined had an overall reported fracture rate of [1/17,000] and a reported symptomatic fracture rate of [1/141,667].<sup>565</sup> In contrast, RNF’s overall reported fracture rate was [1/600] and the reported symptomatic fracture rate was [1/5,100]. Further, the December 17, 2004 HHE, the sixth of the year, with 76 reported serious hazards was also conducted by Bard’s Dr. Ciavarella, and had the following conclusion (underlining added for emphasis):

*○ Reports of death, filter migration (movement), IVC perforation, and filter fracture associated with Recovery filter were seen in the MAUDE database at reporting rates that were 4.6, 4.4, 4.1, and 5.3 higher, respectively, than reporting rate for all other filters. These differences were all statistically significant. Recovery’s reporting rates for all adverse events, filter fracture, filter migration, and filter migration*

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<sup>563</sup> BPVE-01-00617777

<sup>564</sup> BPVE-01-0037344

<sup>565</sup> BPVE-01-000245369; BPV-DEP-00004730

deaths were found to be significantly higher than those for other removable filters.

○ These reported adverse event rates were analyzed in conjunction with a bench test performed at BPV. This test measured “migration resistance” in a simulated IVC. Recovery filter had the lowest mean migration resistance (50 mm Hg), just below that of the removable Tulip filter (55 mm Hg). Linear regression analysis showed a significant inverse correlation . . . of reported migration rates to the migration resistance values in the bench test.<sup>566</sup>

451. With all the information accumulating about the unsatisfactory performance of the RNF after only one year of sales in the United States for retrieval, (FMR January 2004), Bard needing to develop Crisis Management plans, Remedial Action Plans, Sales Force Communiqués after reports of patient deaths, having to hire an outside public relations firm to address the issue, Bard continued to sell the RNF in the United States. As discussed below, in April 2004, Bard was already developing the modifications for RNF to create multiple next generations of products to be sold with piecemeal improvements to rekindle physician interest for the faulty RNF platform and retrieval.

452. Mr. Uelmen testified about Bard’s policy at that time:

*We would stop selling that device if we determined that the risk was greater than anticipated and that it was greater than what we considered the benefits of the device to be.*<sup>567</sup>

453. Based on that statement, there is no explanation why Bard continued to sell the RNF particularly when it already sold the SNF as a permanent IVC Filter. Just having to conduct six HHE for the RNF in the first year of full market release, having received reports of deaths, it had a duty to discontinue sales and notify physicians of the risks for implanted patients. Then in February 2004 when it determined the GFO commercial RNF did meet its predetermined acceptance criteria of 50mm Hg specification, the value in its cleared K022236, it identified the product was violative. Violative product cannot be marketed as safe and effective and it must be recalled. At the minimum, Bard was required to remove all existing inventory “out of specification” from the field to protect public health.<sup>568</sup> Such a public action would have prevented patient injury, notified physicians and FDA of the risk and allowed Bard the opportunity to perform adequate testing of the design and development of an IVC Filter to ensure it performed as substantially equivalent to the SNF.

454. Relatively quickly, physicians began to independently determine there were performance issues with the RNF after implanting the filters in patients, patient injuries and deaths, and difficult or failed attempts at removal.

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<sup>566</sup> BPVE-01-01019821

<sup>567</sup> Uelmen depo Vol I, p198, l. 2-21

<sup>568</sup> 21 CFR 806

455. The public relations firm contracted by Bard, Hill and Knowlton, identified Dr. G. Cohen of Temple University as an External Resource for Bard to use in its Crisis Management Plan. He would support to the press and media the necessity and benefit of the IVC filter for patient care. Dr. Cohen was a user of the RNF with an annual volume of \$250,000. However, he had represented in his comments recorded by his IR Sales person, Magee Ammerman: “Concerned with fracture, migration, tilt, level 1 trauma.”<sup>569</sup>
456. Using post-marketing adverse event reporting for the RNF for fracture data as of December 1, 2005, and assign a hazard rating of 6. The Addendum to BPV’s Remedial Action Plan (RAP) SPA 04-04-01 was revised December 1, 2005, described the reporting of Limb Fractures of RNF:

*BPV addressed the RNF fractures by enhancing several dimensional attributes of the product. The product improvements resulted in the next generation of RNF, the G2 model, product catalogue number RF310F. The G2 has received FDA 510(k) concurrence on August 29, 2005 and has been commercialized in the US since September 8, 2005. With the initiation of sales of the G2 product, sales of the older version RNF were discontinued at the end of September 2005. It is anticipated that the rate of filter fracture will decline with the introduction of the G2 filter, those rates are being monitored by BPV at this time. Reports of filter fracture for both the RNF and the G2 filters are reviewed by senior management of the business each month in Management Board meeting.*<sup>570</sup>

**X. BASES FOR OPINION #4: BARD DEVELOPED ITS “NEXT GENERATION” OF IVC FILTERS BASED ON PIECEMEAL REACTIVE MODIFICATIONS TO ITS FLAWED ORIGINAL RNF FILTER PLATFORM RATHER THAN USE QUALITY SCIENCE AND MEDICAL DEVICE DESIGN PRINCIPLES.**

Bard provided inaccurate and misleading information to the FDA, physicians, and the public regarding the safety and efficacy of its RNF permanent and retrievable filters. Despite its marketing claims, the later iterations of its IVC filters continued to rely on the original flawed RNF platform, but now used as a predicate device. Bard’s IVCF practices overstated benefits and downplayed risk with the introduction of each new member of its commercial family of filters. IVCF changes were made in a piecemeal and reactive fashion heaped onto a flawed underlying RNF platform with a goal to address physician perceptions about improvement to the prior generation of product. Use of new tradenames inaccurately implied improved quality from the prior generation. Based on the internal documents and employee testimonies reviewed, Bard’s evolution of changes starting with the RNF were not primarily made to improve quality, safety, and efficacy or to protect patients but rather primarily to address sales force and physician perceptions about device problems and help keep and expand market share.

<sup>569</sup> Hudnall Exhibit 35; BPVE-01-00177

<sup>570</sup> BPVE-01-00268259

**Applicable Regulations:** 21 CFR § 820.198; 21 CFR § 820.30; 21 CFR § 820.100; 21 CFR § 820.75; 21 CFR § 820.250; 21 USC § 352(a)(f)(1)(2)

**A. BARD’S G2 filter system—the “Next Generation.”**

**1. Bard was proposing the redesign of the RNF as the next generation G2 in 2004.**

457. Bard’s April 1, 2004, Recovery Initiatives with RNF and Recovery Cone<sup>571</sup> proposed the RNF redesign to deal with physician concerns with complications with the RNF and to create new products for marketing to sell. Bard was also working in 2004 on a redesign of the Recovery Retrieval System for RNF.<sup>572</sup> On August 25, 2004, the “next generation” IVC Filter—still based on the RNF filter platform—was introduced with new features to try to help minimize problems with migration and arm fracture. To help improve retrieval of the G2, Bard proposed adding a new retrieval snare (hook) to the G2 filter. Bard also proposed the clearance of a new G2 femoral delivery system.

**2. Physicians began to stop using the RNF based on its poor performance in patients.**

458. Bard listed for its G1A Recovery “Discussions” Customer-PRIORITY, that accounts (physicians/hospital) had stopped using the RNF. From the Western Region sales district came that sales were receiving the following comments about the RNF:

*Heard of [ ] migration and won’t use; recurrent PE resulting in death; [ ] letter and fear of migration; acct has stopped using due to several reported complications; competitive threats; stopped using ; migration; stopped using; concerned about reported incidents; standard of care no longer Recovery; concerned about patient safety; one of first physicians to receive [ ] memo. Has not used it since; had a filter fracture and seen several arms outside the caval wall; heard of [ ] migration and won’t use; failed removal due to tilted filter in young patient; recurrent PE resulting in death; heard of [ ] migration and leery; using Recovery less; using recovery less; stopped using, migration; concerned over bad press; slowed usage dramatically; stopped using.<sup>573</sup>*

**3. Bard in 2008 still had failed to conduct adequate studies to predict the dynamics and environment of a living human IVC and relationship to the survival of implanted Bard IVC filter. .**

459. Despite Bard’s aggressive marketing to physicians, in an internal May 6, 2008 PowerPoint presentation by BPV titled “Filter Franchise Review” with the stated “Objective: Increase Revenue and Capture More Market Share,” Bard listed among its known weaknesses in 2008 that

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<sup>571</sup> BPVE-01-00268911

<sup>572</sup> BPVE-01-00316941

<sup>573</sup> Hudnall Exhibit 35; BPVE-01-00177

it “lacked an understanding of dynamics of caval anatomy-impacting testing methods” and had “limited understanding of user needs.”<sup>574</sup> This “lack of understanding” was never conveyed to the FDA or physicians by Bard, rather Bard portrayed its IVC filters as the safest on the market and itself as a leader in research and knowledge about the use of IVC filters.<sup>575</sup>

**4. Bard in April 2004 Presented Plans to create multiple staggered Next Generations of modified RNFs (G1A, G2 & G3), while continuing to sell the defective RNF.**

460. In conflict with what Bard’s management was telling its Interventional Sales force, physicians, and FDA in 2004 about the adequacy of RNF performance when compared to other commercial IVC filters and the predicate SNF, Bard’s PowerPoint Presentation represents commercial RNF performance differently. The presentation was titled “BPV/Angiomed New Product Development Review Meeting of April 26, 2004.” It showed that Bard R&D had already begun developing a series of next generation modifications of the RNF. Bard wanted address physician perception and issues of migration resistance, hook and radial strength, risks of fracture and tilting. Bard knew as early as 2002 before 510(k) clearance—omitted from its response to FDA’s Question #1 (above) for K022236—that RNF’s tilting, now being reported with commercial filters, compromised both the efficacy and safety of the RNF as a permanent filter for prevention of PE. Tilting reduced clot capture for reduction of PE, the reason it was implanted. Tilting also reduced filter safety, increasing the risk for perforation, fracture and migration. Bard was also already working on a redesign of the retrieval system for RNF.<sup>576</sup> The April 26, 2004, presentation was a joint presentation with members of Bard’s Angiomed. Bard had created a series of staggered and reactive modifications for the NMT RNF platform to address physician concerns. Staggering the changes helped keep a stream of new filters for Bard’s sales force to promote. The products were identified as G1A, G2 and G3<sup>577</sup> in the presentation by Rob Carr and Alex Tessmer. These proposed modifications of RNF would eventually get cleared by FDA as modification of a predicate flawed RNF rather than the SNF.

461. The Recovery Filter proposed for next generation was “G1A R002-Migration and R002-fracture,” for the G1A filter. FIR/R002 History Review (G2 Express, G2, RNF)<sup>578</sup> Bard planned to obtain clearance of a Recovery G2 Filter delivered by a new femoral insertion route. Eventually, it would have the ability to use a new snare for G2 filter retrieval and then take measures to address issue R002-fracture. There was already a plan to go ahead with a Generation 3, (G3) filter, by use of a contract to an outside development group.

462. According to Bard’s VP QA Chad Modra’s testimony, the G2 filter changes were not intended to directly deal with migration. And changes for migration did not occur to 2009 and the Meridian Filter.<sup>579</sup> However, the modifications made to the RNF to create the G2 do not fully support his

<sup>574</sup> BPVE-01-00622862, Tessmer Exhibit 14

<sup>575</sup> BPV-17-01-00098021

<sup>576</sup> BPVE-01-00316941

<sup>577</sup> The April 2004 proposed RNF modifications were sold by the following tradenames G1A=G2 IVC Filter, G2=G2 Express IVC Filter, G3=Eclipse IVC Filter (also referred to internally by project name: Vail Filter).

<sup>578</sup> BPVEFILTER-01-00003802

<sup>579</sup> Modra deposition 6/6/14, p. 95-96, L. 1-19

statement. The trends for filter modifications by Bard's R&D Engineering were directed towards improving migration resistance to initially resemble the SNF. The changes were intended to have the migration resistance of the G2 fall into the mid-range of comparable filters >80mmHg migration resistance. The upper filter arms were modified to be longer than the RNF, a significant lengthening of 12mm to 18.75mm. The G2 had modifications more closely resembling the SNF (rather than the RNF) to help address stability (improved migration resistance).

463. The migration of the RNF had been both cephalad and caudal and there was an association with motion and tilt. The G2 proposed changes to increase the size of the anchoring leg hooks, increase the leg span to 40mm, and use longer upper arms. The goal of the next generation filters as described in 2004 was to address three issues: #1) Retrieval, #2) Deployment, and #3) Surface finishing (facture). The changes were to respond to physician recommendations and perceptions about the filter which would benefit marketing the filters to physicians and not with a stated purpose for protecting patients and improving safety. However, the changes were consistent with a pattern of piecemeal reactive changes made by Bard in response to the surfacing of physician concerns.
464. A primary goal of the next generation IVC filters was to continue to use a filter based on the RNF platform but introduce delivery by a "femoral delivery system." The RNF had been delivered by the jugular /subclavian kit. When the G2 was eventually cleared for retrieval by FDA in 2008, only then was a top hook added for retrieval and the product sold as the G2 Express. The third goal was surface finishing to help address risk of fractures (corrosion, surface pitting, imperfections, R002-Fracture). To accomplish better filter surface finishing, Bard introduced a standard medical device metal surface passivation process called electropolishing. At first the electropolished product was sold by the trade name 'G2 Platinum' but then later it was renamed and sold as the Eclipse IVC Filter. (See discussion below of Eclipse).

**5. Bard's R&D engineers initially sought to improve migration resistance of G2 to be like SNF but obstacles got in the way.**

465. Bard's R&D engineers made early improvements for migration resistance but were not able to complete the task as initially planned based on conflicting company concerns about cost and profits.
466. Internally, Bard's Quality Assurance (QA) initial specification for the second generation "G2" showed Bard's R&D engineers had thought of changes which would improve migration resistance for the new G2 filter design. This was partly based on the successful commercial history of the SNF with higher migration resistance, as well as Bard's competitive in vitro filter testing showing a higher migration resistance at >80mmHg for competing IVC filters as a permanent filter than the RNF with the minimum 50mmHg value. The migration resistance acceptance specification for the G2 was initially proposed as equal to or greater than the SNF. Bard R&D was apparently aware in 2004 that performance of the RNF as the G2 could be improved if there were certain changes to the G2's design to help create a shift more towards a middle range of migration resistance (>80 mmHg @ 28mm) as seen with competitors. Bard

R&D's plan for the prior G1A filter was to "Address Filter Migration" with a new acceptable resistance specification of at least ">80mmHg @ 28mm tube."<sup>580</sup> This would still be lower than the SNF but place the next generation commercial G2 in a middle range of migration resistance competitive with other commercial IVC Filters, but still greater than the flawed RNF.

467. Bard's testing of January 13, 2005, the Modified RNF (G2) was shown not to be able to meet the initially proposed product performance specifications of migration resistance testing in the 28mm tube (equal or better than the SNF). The February 10, 2005 Product Performance Specification (PPS070028) Next Generation Revision,<sup>581</sup> draft 3, the G2 failed to meet initial performance specification for migration resistance (equivalent to or better than the SNF) and showed a lower radial leg strength. The difference in migration resistance between the SNF and G2 was determined to be statistically significant. G2 migration resistance was less than the SNF but still greater than the RNF.<sup>582</sup> Bard's ETR-05-02-05 was titled "G1A RNF Femoral System Design Verification & Validation Report Project #8027- Migration Resistance."<sup>583</sup> As will be discussed further, the Bard Product Performance Specification Next Generation Revision 2 had the specification for migration resistance of the G2 changed to an acceptance criteria of greater or equivalent to the RNF (50mmHg).<sup>584</sup>

468. There was discussion that Bard engineers should also make efforts to help reduce the scrapping of materials like Nitinol used to produce G2 filters to help translate into reduced costs for Bard and increased profits. Each time Nitinol material for a G2 filter needed to be reworked (based on a failure to meet specifications or acceptance criteria in production), it was known that migration resistance of the final released finished filter would also be decreased proportionately to number of reworks. The more the reworking of the materials, the lower the migration resistance of the final product. Bard's engineers were asked to determine how many times the same filter materials could be reworked in-house to make a G2 filter, yet, still produce a commercially releasable G2 filter. If Bard's R&D changed the migration resistance as proposed to a higher >80mmHg (still not the SNF) that would reduce the number of times G2 filter materials could be reworked in-house. The G2 design changes in general were considered by Bard's engineers an improvement over the original RNF based on migration resistance. If Bard's migration resistance specification remained unchanged at the RNF's 50mmHg specification, (the predicate used for the G2 510(k) clearance and value stated in FDA's 510(k)), a G2 filter could be "reloaded" (reworked) up to five times and still be able to be released by Bard's minimum release criteria of 50 mm Hg.<sup>585</sup>

469. In the G1A Fact Book and in a presentation made by Bard's Quality Assurance staff, under rework and in association with Bard's qualification of a new Nitinol wire supplier (New England Precision Grinding),<sup>586</sup> Bard compared migration resistance of the G2 made with a new Nitinol

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<sup>580</sup> BPVE-01-00316941

<sup>581</sup> BPVE-01-00004497.

<sup>582</sup> BPVE-17-01-00001134

<sup>583</sup> BPVE-01-00272936

<sup>584</sup> BPVE-01-00272936

<sup>585</sup> BPVE-01-00316941

<sup>586</sup> BPV-17-01-00120904 G1A Fact Book Project #8027

wire supplier with multiple reworks to both the SNF and RNF. By Bard's bench testing, the highest migration resistance was consistently measured for the SNF [range: 113.6-121.8mmHg] For a series of G2 productions using the new Nitinol supplier and measuring migration resistance at 1X (first production)[range: 85.2-92.5mmHg] > than 5X rework [range: 75.4-83.2mmHg] > RNF [(range 55.8-56.3mmHg)].<sup>587</sup> The conclusion of Bard's analysis of the G2 Nitinol wire supplier's testing was that maintaining the migration resistance specification at the 50 mmHg value of the RNF would permit release of a G2 IVC filter with improved migration resistance compared to the RNF and permitted the cost savings of the option to use five reworks:

*New England Precision Grinding provides ground wires with acceptable migration resistance*

*5 times loaded filters provide acceptable migration resistance*

*Manufacturing process specification for loading filter will remain 5X maximum*<sup>588</sup>

*Cost per unit when scrapped at loading: RNF=\$140.61 versus G1A(G2)= \$120.78.*

*Cost savings for current 1800 manufactured G1A units: \$7593 (3%) - \$12,655 (5%).*

*Cost savings per year (assuming 2000 units per month)- \$101,239.20 (3%) - \$168,732 (5%).*<sup>589</sup>

470. Therefore the G2 production continued to use the 50mmHg of the RNF as the specification for acceptable migration resistance release.

**6. FDA independently contacted Bard in 2005 regarding concerns about an FDA-detected safety signal for RNF and after reports of serious adverse events and deaths in Recovery Filter-implanted morbidly obese patients.**

**a. FDA's Nurse Consultant identified a 'postmarket safety trend' for Bard's RNF in FDA's MAUDE database.**

471. On January 21, 2005, a Contact Report was written by Bard's Sheri Allen, which relayed a discussion she had with FDA's ODE reviewer Lisa Kennell regarding Bard's submission of its next 510(k). Ms. Allen recorded that she mentioned to Ms. Kennell that Bard may consider voluntarily opening a clinical registry for its commercial IVC Filters to obtain post-market performance data.<sup>590</sup>

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<sup>587</sup> *Id.*

<sup>588</sup> *Id.*

<sup>589</sup> *Id.*

<sup>590</sup> BPV-17-01-00102065

472. Ms. Allen made a later February 4, 2005, FDA Contact Report involving FDA's Lisa Kennell, "Subject: Recovery Filter-Update." Ms. Allen had telephoned Ms. Kennell at CDRH to determine if she had finished her review of Bard's DRAFT customer letter she had emailed to her on January 21, 2005. Ms. Kennell indicated that she had been sick, she thought the letter looked good and had no comments. She also told Ms. Allen to go to Ms. Jenny Liu (Office of Surveillance and Biometrics (OSB) in the Office of Compliance (OC), a postmarket arm that reviews submitted Medical Device Reports (MDRs) with Bard's proposed draft Dear Doctor letter:

*That Jenny Liu, who is responsible for reviewing Medical Device Reports (MDR) at the FDA, observed an increased trend about the same time as I contacted Ms. Kennell on January 21, 2005. ...Ms. Kennell indicated that Ms. Liu would probably be the best person at FDA to review the proposed customer letter...*

*I told Ms. Kennell that we are still working on development of the study design for the post-market registry. ....I told her that we still plan to seek her review of the protocol upon completion of a solid DRAFT.*

473. Ms. Allen wrote another FDA Contact Report now dated February 8, 2005, regarding an interaction Ms. Allen had with FDA's Jenny Liu, RN, MSN, Nurse Consultant, Division of Postmarket Surveillance, Office of Surveillance and Biometrics (OSB), CDRH. Ms. Liu had contacted Ms. Allen and told her that she was the individual responsible for reviewing MDRs at FDA and that she was contacting all three cleared retrievable IVC filter manufacturers in the United States to obtain additional information about the products since she had identified an increasing trend in FDA's receipt of MDRs for retrievable filters, particularly filters used in bariatric patients. Ms. Allen continued in her note:

*She indicated she had observed an increased trend in MDR reportable events for all retrievable filters, especially in bariatric patients. She said she believes that this is because the retrievable indication provides a treatment option for new patient populations, including bariatric patients...*

*I asked Ms. Liu if she had received a copy of the proposed customer letter from Lisa Kennell in the FDA office of Device Evaluation (ODE). She said she had not received it, but she will follow up with Ms. Kennell....I also told her that we plan to convene an expert panel of bariatric surgeons on Saturday, February 12, 2005, and we would really like to receive her input prior to this date.<sup>591</sup>*

474. Ms. Liu then faxed Bard's Ms. Allen a February 8, 2005 letter officially requesting Bard provide FDA with additional information within 5-days to help her complete the agency's review of retrievable IVC filter Medical Device Reports (MDR).<sup>592</sup> Ms. Liu wanted information to help her differentiate MDRs for Bard's permanent Recovery Filter (K022236) versus Bard's Retrievable

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<sup>591</sup> BPV-17-01-00000208-11

<sup>592</sup> BPV-17-01-00058076

Recovery Filter System (K031328).<sup>593</sup> She also requested Bard provide her with the total number of Recovery Filters that were distributed in the United States for the last 3-years (denominator for risk calculations). She also requested the Recovery sales data be further broken down into 6-month periods as to the volume and type of Recovery device (permanent vs retrievable). Finally, she wanted Bard to send her a sample of Recovery device packaging, advertising and promotional materials for both Recovery Filter Systems (K022236 and K031328) (permanent and retrievable).<sup>594</sup>

475. Ms. Liu then contacted Ms. Allen on February 14, 2005, following her receipt of a copy of Bard's draft proposed Recovery Filter System customer letter that she, Ms. Liu, obtained from Ms. Kennell in ODE.<sup>595</sup> Ms. Liu indicated that she was the appropriate person at FDA to help coordinate FDA's review of the draft letter not a member of ODE premarket staff. She also wanted to provide clarification for her February 8, 2005, requesting additional information from Bard. Ms. Allen told Ms. Liu that based on the Bariatric Surgeon Expert Panel meeting and a survey, Bard was going to revise its proposed Bard draft dear doctor letter. Ms. Liu then requested Ms. Allen provide her with a summary of the Bariatric Surgeon panel meeting. Ms. Allen provided her a summary of meeting highlights, including that the consensus was that morbidly obese patients should be considered as a high-risk patient group rather than focus only on IVC filter use in bariatric surgery patients. Ms. Allen continued:

*Morbidly obese patients may be at greater risk of developing DVT because of several factors including weight (>400lbs), body mass index (BMI), biochemical abnormalities, and heightened inflammatory response. These patients may also be more prone to developing larger clots, which could distend the Inferior Vena Cava (IVC) and result in dislodgement of the filter. Additionally, it is difficult to recognize clinical symptoms (e.g. edema) of DVT in obese patients.*

*...It is difficult, if not impossible, to measure the IVCs of morbidly obese patients, as many of these patients will not even fit into a CT scan.*

476. Ms. Liu inquired if IVC Filter use in trauma patients had been discussed. She also inquired if Bard intended to make any IVC Filter device modifications to the Recovery to address filter migration.

477. Ms. Allen wrote that she told Ms. Liu, Bard was making specific dimensional changes that might help reduce migration and fractures. She continued:

*I asked Ms. Liu is(sic) she has reviewed the table we provided to Lisa Kennell in October, which identified the complication rates, based*

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<sup>593</sup> BPV-17-01-00058076

<sup>594</sup> BPV-17-01-00000208-11

<sup>595</sup> BPV-17-01-00025340

*upon sales, while in the context of the Society of Interventional Radiology (SIR) Quality Improvement Guidelines.<sup>596</sup>*

*I closed the discussion thanking Ms. Liu for her time and telling her that I will send a response to her questions soon.<sup>597</sup>*

**7. Bard Inappropriately References SIR Guidelines as Support for Acceptable Performance of Its New IVC Filter.**

478. The published SIR threshold data for permanent IVC filters (Grassi 2003) was repeatedly taken out of context by Bard in its QA documents, communications with FDA, with its own sales force. The SIR Guidelines were not intended as a truly valid or meaningful comparison for quality assurance by industry to support adequate Recovery Filter (or G2/Eclipse Filter) IVC filter design and performance. The guidelines were intended for use by physicians implanting IVC filters. Dr. Grassi, the lead author for the published SIR Guidelines testified that the SIR thresholds were not intended to provide acceptable ranges of adverse events reported by manufacturers to support adequate device performance of an IVC filter design and production. Dr. Grassi's response when asked to describe the role of the SIR Guidelines:

*A. And certainly I can say that in the quality improvement guidelines for IVC filter placement through SIR for which I was the first author, we did not imply that rates in that range are fine or acceptable or okay. We simply said that those were trackable events and that responsible individuals should look at any adverse event, trigger a review, and do a quality assurance monitoring to make sure that they understand some root causes behind such a serious problem.<sup>598</sup>*

Dr. Grassi also testified that for an investigation of adverse events for Bard's IVC filters:

*He would want to know the summary of an investigation....*

*Well, what I can say in the general sense is that personally and many of my colleagues would logically seek the device with the greater benefit and the fewer risks or complications.<sup>599</sup>*

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<sup>596</sup> SIR Guidelines; Grassi CJ, Swan TL, et al., For the Society of Interventional Radiology Standards and Practice Committee, Quality Improvement Guidelines for Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism, *J Vasc Interv Radiol* 2001, 12:137-141; Grassi CJ, Swan TL, et al., For the Society of Interventional Radiology Standards and Practice Committee. Quality Improvement Guidelines for Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism, *J Vasc Interv Radiol* 2003; 14: S271-S275

<sup>597</sup> BPV-17-01-00025340-2

<sup>598</sup> Grassi deposition 8/27/14, p. 525-6, L. 14-1

<sup>599</sup> Grassi deposition 8/27/14, p. 534-5, L. 16-21

479.

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481. The Special 510(k) for the Recovery G2 as submitted by Bard on March 2, 2005 was assigned K050558.<sup>604</sup> On March 14, 2005, the FDA sent Bard a list of FDA's questions it hoped Bard would address during a presentation for a planned March 2005 meeting. Bard was told that the FDA was planning to bring 13 agency attendees from different areas of CDRH and the FDA Post Market Investigation (PMI) team and there had been two internal meetings of this PMI group prior to the scheduled meeting on the topic with Bard. The Agency's questions in the letter were divided by FDA into two distinct categories: #1) Survey Specific Questions (4 questions); and # 2) Device Related Questions (9 questions). FDA asked Bard to address 'post-market risk issues' including clarification of the "no time limit" recommendations for retrieval, and perceived filter

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<sup>600</sup> BPV-17-01-00045862-922

<sup>601</sup> BPV-17-01-00045862-922

<sup>602</sup> BPV-17-01-00045862-922

<sup>603</sup> *Id.*

<sup>604</sup> FDA\_PRODUCTION\_00000048

risks. The FDA asked if Bard was intending to “establish a device registry” to gather post-market data on the Recovery filters. Ms. Kennell had addressed this meeting in her March 29, 2005, “ODE Review Memorandum (Decision Making Document is Attached).”<sup>605</sup>

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[REDACTED]

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[REDACTED]

484.

[REDACTED]

[REDACTED]

485.

[REDACTED]

[REDACTED]

[REDACTED]

486. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

487. [REDACTED]

[REDACTED]

[REDACTED]

488.

489.

[REDACTED]

490. [REDACTED]

[REDACTED]

[REDACTED]

491. [REDACTED]

[REDACTED]

492. [REDACTED]

493. [REDACTED]

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[REDACTED]

**8. Bard submitted its Next Generation Recovery (G2) Special 510(K) to FDA for clearance of the G2 IVC Filter with a new femoral delivery system.**

494. As stated above, Bard submitted a new Special 510(k) for Design Modification of its RNF it called the Recovery G2 Filter with Femoral Delivery on March 2, 2005, before the March 24, 2005 PMI meeting with FDA. Bard's Special 510(k) cited the RNF as the predicate (cleared by K022236 and K031328). The Special 510(k) K050558<sup>622</sup> would be cleared on August 29, 2005 by FDA as only a permanent G2 IVC Filter. Without describing the postmarket safety issues occurring with the Recovery IVC Filter nor discussing the significant differences between the RNF and the SNF predicate device, Bard's 2005 Special 510(k) for the G2 provided support from Bard that the commercial safety and efficacy history of the RNF had been acceptable when compared to the SNF as a permanent filter and the RNF could now be referenced by Bard for its proposed G2 based on "substantial equivalence."

495. On the 510(k) Reviewer Summary signed-off by Lisa Kennell on March 29, 2005,<sup>623</sup> under "Comments" she describes FDA's awareness (but not knowledge of the source) that there is "off label" use in obese patients, knowledge that changes were made to increase migration resistance and reduce filter arm fractures. She knew that the "previous animal and bench testing did not reveal problems with migration" but that "the bench and animal testing was not predictive of clinical failure." She also was aware that the "modifications made to the existing design had resulted in problems with retrieval." Bard had already committed to conducting a 300-patient clinical trial to capture clinical data on its modified G2 filter (underlining added for emphasis):

*Comments*

*Changes were made "as a result of continued product improvement with the possibility of increasing filter migration resistance and reduction of filter arm fractures." However, I believe that the changes are being made to address serious adverse events (some results in death) in a sub-population in which the devices are being used "off-label." The firm submitted information to FDA via official (add-to-file) and unofficial (i.e. via electronic message) modes relating to IFU modifications, "Dear Doctor" letters, surveys, and meetings that have been held to discuss this development (see information attached). The "off-label" use is for prophylactic placement, possibly without measuring IVC diameter, in obese patients who are to undergo gastric bypass or other procedures. This subset has been experiencing migration and fracture of the device, with serious, sometimes fatal, consequences, and the device has been causing the very complication it was placed to prevent. We held two PMI (Post-Market Investigation) meetings, and a meeting with the firm on march 24<sup>th</sup> to discuss the development and outcome of the surveys.*

<sup>622</sup> FDA\_PRODUCTION\_00000048; BPV-FULLER-000005718

<sup>623</sup> FDA\_PRODUCTION\_00000048 at 00000217

*The firm has also proposed a post-market study to assess migration in this subset of patients....*

*...Competitor devices have time limit stipulations in their labels, because after the healing-in process, they cannot be removed because the vessel is damaged. I would therefore recommend that the submitter conduct a small 'proof of concept' study to determine if there should be a maximum implant period, or if the current label with no such limitation is still appropriate.*

#### **Addendum**

*The PMI team met with the firm on 3/24/05 to discuss the adverse event reporting overview, design changes and validation testing, data-gathering and findings, and next steps. ...Based on feedback from users, the firm has decided to conduct a post-market study of 300 patients at 30 sites to capture data on migration and fracture. This group will include a mixture of subjects including obese, trauma, and young as well as those who are currently indicated. Patients will be followed for 12 months, or for 1-month post-retrieval, whichever comes first.<sup>624</sup>*

496. Ms. Kennell provided in her note what she had been told by the CDRH 510(k) staff about the limited options available to FDA's ODE reviewers regarding addressing a safety risk of off-label use of IVC Filters in obese populations. Issues of off-label use are usually viewed more as a post-market issue to be dealt with by Office of Compliance, not ODE. Ms. Rosencrans did not suggest to Ms. Kennell that ODE bring in others members of OC to help address Bard's off-label use. If it could be shown that Bard was promotion of encouraging off-label use, that would open up additional post-market regulatory actions for Bard's marketing outside of the limited role of ODE:

*I met with Heather Rosencrans on 3/22/05 to discuss what we could not request for special 510(k)s. I was advised that we cannot ask for bench, animal, or clinical data that specifically addresses the issues identified in the obese population since this is an "off label" use. Therefore, any studies we request will need to involve only the population for which it is labeled. A post-market study for obese population can be conducted if the company opts to, or if required by OSB under the 522 provision of the regulation. At best, we can only clear the device with limitations. In anticipation of such a clearance, we should ask that the label be modified to contain the limitation statement.<sup>625</sup>*

497. On March 30, 2005 FDA, six days after the March 24, 2005 PMI meeting, the agency sent Bard a letter requesting additional information for the G2 510(k). In terms of the animal studies that had been submitted for the 510(k), FDA wanted to see a histology assessment and both

<sup>624</sup> FDA\_PRODUCTION\_00000048 at 00000215-218

<sup>625</sup> FDA\_PRODUCTION\_00000048 at 00000215-218

representative slides for the implanted new device and comparative slides to the implanted predicate. FDA wanted a small “*proof of concept*” clinical study (humans) to assess whether or not the current label (i.e. no retrieval option) was still appropriate for the G2’s clearance. FDA wrote: “*Such a study should assess migration of the device. In the event that obese patients were enrolled into this study, data from the subset should be presented separately as well as pooled. We would be happy to review a protocol under pre-IDE, if you want to submit one.*”<sup>626</sup>

498. FDA’s Question #3 was a request for Bard to voluntarily add a specific new boxed warning to the IFU. It was to warn against use of the Recovery IVC filter in morbidly obese patients and notify the physician of the risk of death for the Recovery Filter System IFUs based on receipt of post-market adverse events including death. FDA also requested Bard add a new warning to the IFU warning about risk for fracture and migration in patients with central venous lines:

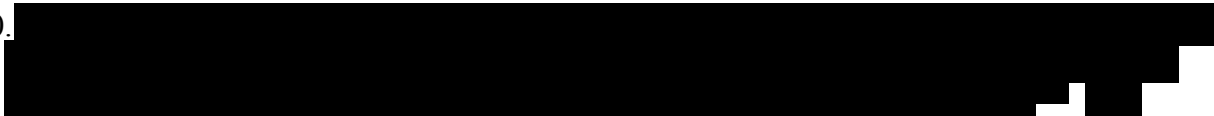
*Any marketing clearance of this modified device may be considered “substantially equivalent with Limitations” given the adverse events observed in obese population. As such the IFU should be modified as follows:*

- *Add a boxed warning at the beginning of the “Warnings” section that states the following: Warning: The safety and effectiveness of the Recovery Filter System in morbidly obese patients has not been established. There have been fatal device-related adverse events reported in this population.*
- *Add a warning that central venous lines may cause the filters to move or fracture.*<sup>627</sup>

499.



500.



<sup>626</sup> FDA\_PRODUCTION\_00000048 at 00000067

<sup>627</sup> FDA\_PRODUCTION\_00000048 at 00000067

<sup>628</sup> Hudnall Exhibit 12

<sup>629</sup> Barry Exhibit 5

501.

502.

503. At the May 6, 2005 Teleconference, Dr. Buckles noted that FDA was concerned whether the modifications (hook dimensions) to improve migration & fracture AEs would adversely affect the long-term retrievability. He also said that FDA could not determine substantially equivalent of the long-term retrievability without pre-clinical data. Ms. Smith was recorded as saying “she expressed concerns that Bard has not specified at time limit for retrieval in the IFU. She also stated that FDA will consider a proposal for acute retrieval up to 3-4 weeks.”<sup>630</sup>

504. According to a June 3, 2005 response letter from Shari Allen, BPV to Angela Smith, FDA, in a May 6, 2005 teleconference “FDA indicated it did not have enough data in the Special 510(k) to determine if the modifications to the RNF might affect the filters long-term retrievability.” FDA indicated that they would consider a proposal for “acute retrieval up to 3-4 weeks,” however, the 510(k) for the change in indication would “require a traditional 510(k).”<sup>631</sup> During a subsequent telephone conversation on May 27, 2005, FDA indicated that a request for “retrieval up to 3-4 weeks would not be accepted without clinical data.” So, on June 3, 2005 Bard was intending to

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<sup>630</sup> FDA\_PRODUCTION\_00000048 at 00000285

<sup>631</sup> FDA\_PRODUCTION\_00000048 at 00000280 at 000000282

file an Investigational Device Exemption (IDE) to conduct a clinical study to assess the safety of removal of the Recovery Filter.<sup>632</sup>

**a. Bard Submitted IDE For ‘EVEREST’-G2 Retrieval**

505. [REDACTED]

506. [REDACTED]

[REDACTED]

507. [REDACTED]

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<sup>632</sup> FDA\_PRODUCTION\_00000048 at 00000280 at 000000282

<sup>633</sup> BPB-17-01-00056051

<sup>634</sup> *Id.*

<sup>635</sup> BPVE-01-00030385; BPV-17-01-00131662

<sup>636</sup> BPV-17-01-00045007

<sup>637</sup> BPV-17-01-00045007

508. FDA ODE was aware that Bard had made changes to the G2 to help address the reports of migration. A May 2, 2005 Review from Victoria Hampshire, VMD, PVDB, ODE sent to ODE Reviewer Lisa Kennell. She recorded she was told by Bard that improvements made to help prevent migratory adverse events were a “more elastic hooked foot and longer arms”:

*Bard has made modifications to this device to try to prevent migratory adverse events. Engineering adjustments to this device over the predicate devices (K894703, K912144, K940489, K963014, K963016) include a more elastic hooked foot and longer arms.*

**Conclusions**

*Review of the MAUDE database and the available medical literature indicates that the post approval period of IVC filter devices (Bard and other) frequently describes adverse event-related perforations, broken, and/or migrated device. The literature reveals that humans vary in IVC diameter depending on height and weight.<sup>638</sup>*

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[REDACTED]

510.

[REDACTED]

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<sup>638</sup> FDA\_PRODUCTION\_00000048 at 000000185

<sup>639</sup> BPV-17-01-00030247; BPVE-01-00195515; BPV-17-01-00000119

<sup>640</sup> Bard Engineering Test Report Number ETR 05-02-11 Rev 0 G1A Recovery Filter Femoral System Chronic Animal Study Report (Project #8027), BPVE-01-00257975

511. Below is the Comparison table in the G2 Special 510(k) intended for the FDA reviewer comparing the new IVC filter (G2) to the predicate RNF:



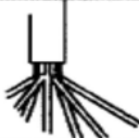
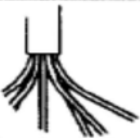
Special 510(k)  
Recovery® Filter System

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**D. Comparison Summary Table**

The Table 1 identifies the similarities and differences between the predicate device and the subject device. The differences are in **BOLD**.

**Table 1. Comparison Summary Table**

	Predicate Device	Subject Device	Modifications
Indications for Use	-	-	None
Warnings	-	-	None
Contraindications	-	-	None
Operating Principle	-	-	None
Sterilization Process and SAL	-	-	None
Filter and Delivery System Materials	-	-	None
Packaging Configuration and Materials	-	-	None
Filter Hook Wire Diameter (nominal)	0.0085"	<b>0.0105"</b>	Increased hook wire diameter.
Filter Leg Span (nominal)	32 mm	<b>40 mm</b>	Increased filter leg span.
Filter Arm Length (nominal)	12.00 mm 	<b>18.75 mm</b> 	Increased filter arm length.
Filter Arms Tips	Tips of filter arms are straight.	<b>Tips of the filter arms are curved</b>	The tips of the filter arms have been curved.
Filter Arm Geometry			Increase in radius of curvature on filter arm at sleeve.
Filter Legs and Spline	The spline has longer	The spline has	Modified spline

Bard Peripheral Vascular, Inc

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**BARD**

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512. In terms of the crucial “*elastic hooks*” of the RNF (and the Ravenscroft NMT Removable US Patents) it was intended to facilitate retrieval. The RNF leg hook was to straighten out with the tug of removal force. The size of the leg’s hook that is ground from the filter wire was changed from 0.0085” (RNF) to the wider “0.0105” (G2) with both cleared as intended as a permanent filter. That was a significant change for the G2 compared to the RNF. The next change based on

<sup>641</sup> FDA\_PRODUCTION\_00000048 at 00000098

the Comparison Table 1. Comparison Summary, the crucial leg span necessary for “proper hook engagement” was also changed without adequate discussion of the risks. The SNF had a leg span of  $36\pm 4\text{mm}$  (32-40mm), the RNF predicate was shown that at  $<32\text{ mm}$  there was loss of proper hook engagement, with the permitted specification for leg span of 30-34mm. The G2 table above has a leg span increased to 40mm (the upper limit of the SNF) with no further explanation as to the combined differences in the leg hook diameter and the new wider leg span.

513. There is no specific and objective discussion of the SNF migration resistance, mid-range of other IVC filters, the medical literature or Bard’s proposed specification of  $>80\text{mmHg}$ . There is no mention of Bard’s practice of “reworking filters” up to five times to avoid scrapping of materials and cutting of costs and still being able to release reworked filters based on a requirement for a minimum 50mmHg specification. Instead FDA is told the “*Subject device must withstand a minimum of 50mmHg pressure in a simulated IVC diameter of 28mm.*”
514. The FDA is given the following footnote information about the SNF, the RNF and the new G2, including information that neither the G2 nor the RNF are equal to the SNF<sup>642</sup> in “Table 3. Design Control Activities Completed for the Subject Device”:

*“The predefined acceptance criteria for this test was inappropriately established to be statistically equivalent to Bard’s Simon Nitinol Filter (SNF). The more appropriate acceptance criteria should have been defined to demonstrate equivalent to or improvement over the predicate device (current Recovery Filter). The subject device did not meet the predefined acceptance criteria to be equivalent to SNF at simulated IVC diameter of 28mm. However, the subject device showed significantly increased average migration resistance (88%) when compared to the predicate device and was found to be statistically greater. Therefore, the subject device met the more appropriate acceptance criteria that should have been the predefined criteria assigned to the test.”*<sup>643</sup>

515. The filter’s radial length strength was compared to the SNF, in the original RNF 510(k), and it needed to be less or equivalent in a 15mm tube. The reason the SNF was chosen was that it represented the worst-case scenario for caval perforation as stated in the RNF 510(k). Bard did not indicate any data from new testing performed on the G2. Filter Respiratory Fatigue Resistance, Bard cited the data already reviewed and included in K022236. Bard’s animal studies were conducted in sheep according to Proctor (2003).<sup>644</sup> The focus of the animal studies was ‘short term implant’ and effects of removing the filter on the vena cava. Bard’s animal testing

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<sup>642</sup> Bard admitted in a footnote that the G2 is not equivalent to the SNF and RNF is not equivalent to the SNF for migration resistance. Bard is implying its awareness that the risk of migration is greater for RNF than SNF. That was not how it was stated in K022236 where Bard told the FDA that both RNF and SNF met the 50mmHg minimum.

<sup>643</sup> FDA\_PRODUCTION\_00000048 at 00000104

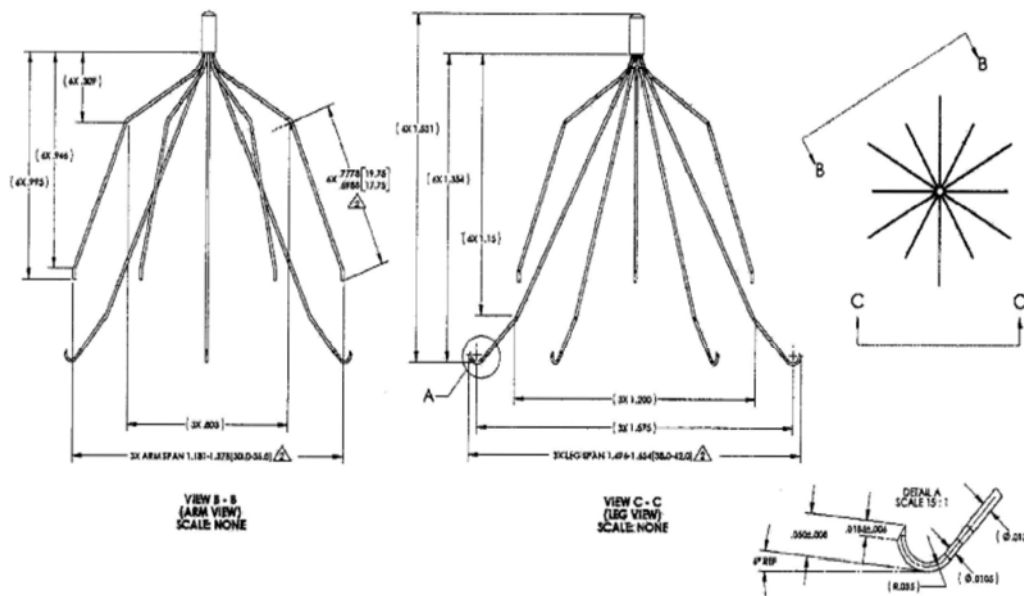
<sup>644</sup> Proctor MC, Cho KJ, Greenfield LI, Development and evaluation of investigational vena cava filters: the complimentary roles of in vitro and in vivo studies. *J Surg Res* Mar. 2003. 110(1), at 241-64.

was not designed to address changes associated with chronic implantation of the finished modified G2. The Declaration of Conformity in the 510(k) was signed by Bard's Avijit Mukherjee, Program Manager, and Doug Uelman, VP QA. Bard's Truthful and Accuracy Statement was signed by Kay Hutchinson.

**Special 510(k)  
Recovery® Filter System**

Page 55

### Subject Device – Filter



516. On July 2005, the FDA sent a letter signed by Bram Zuckerman, MD, Director, Division of Cardiovascular Devices requesting additional information to complete the review. The FDA asked for additional animal data for a permanent filter not for a retrievable filter. The FDA wrote in Question #1: “As you indicate in your cover letter that you are no longer pursuing clearance of the device for retrieval, it is unclear how this data provides assurance of safety and efficacy of the Recovery Filter System as a permanent implant. You should provide additional *in vivo* data or a scientific rationale for why the data presented is applicable to the subject device when indicated as a permanent implant.”<sup>645</sup>

517.FDA's Question #2 requested information about the potential for physicians to confuse the RNF's retrieval option with the FDA's clearance of the Recovery G2 as only a permanent implant. The FDA requested that all reference to the 'Recovery Filter System' be deleted from Bard's marketing materials. The FDA said that the continued use of the trade name 'Recovery Filter System' falsely implied that the G2 was also intended to be retrievable, an off-label use not permitted by 510(k) clearance. To further make this point of distinction between the RNF and G2 and off-label use for retrieval, the FDA continued:

645 FDA PRODUCTION 00000048 at 00000058

*This would be considered off-label use of the subject device as your proposed indication is for permanent placement. As the currently marketed Recovery Filter System is indicated for device retrieval, you should change the name of the subject device to differentiate between the two systems so that the retrievability of the device is not implied. Specifically, you should remove all references to the device as the Recovery Filter System in your Indications for Use, Instructions for Use, 510(k) Summary and Package Labeling.*<sup>646</sup>

518. Ms. Smith wrote a July 26, 2005, review note to the 510(k) file for K050558/S001 and said that *“since device clearance, FDA analysts in the Office of Surveillance and Biometrics have noted a trend in migration and fracture of the Bard Recovery Filter.”* Bard has communicated with the FDA that this trend is most notable in obese patients, especially those having gastric bypass surgery. Adverse events in this patient population have led to death and the need for re-intervention to capture fractured device. While it was uncertain why this population seems to be experiencing higher incidence of adverse events, the *“manufacturer hypothesizes that it may be to the higher stresses placed on the device due to the differences in the anatomy in obese patients or the inability of the physician to appropriately image the size of the vessel pre-implant (it is contraindicated for vessels over 28mm).”*<sup>647</sup>

519. Due to this increased incidence of adverse events associated with the RNF, Ms. Smith indicated that BPV had worked to communicate with the medical device community sending out two Dear Doctor letters, conducting surveys of physicians implanting IVC filters, and modifying its labeling. Ultimately, however, *“BPV believes the device modifications are needed to mitigate the apparent risks associated with implantation of the recovery filter.”* The sponsor submitted a Special 510(k) on March 3, 2005 proposing the following device modifications:

- Increase in hook wire diameter from 0.0085” to 0.0105”
- Increase in filter leg span from 32 mm to 40 mm
- Increase in filter arm length from 12.00 mm to 18.75 mm
- Addition of curve to tips of the filter arms (tips of filter arms were previously straight)
- Increase in radius of curvature on filter arm at sleeve
- Shorten grooves and add waist to spline design

<sup>648</sup>

520. Ms. Kennell wrote in the 510(k) review: *“While the sponsor’s bench testing was adequate to support the modifications, it was determined that additional information regarding the animal study data and a ‘proof of concept’ clinical study would be needed prior to clearance.”* As stated

<sup>646</sup> FDA\_PRODUCTION\_00000048 at 00000058

<sup>647</sup> The ODE non-clinical reviewers were not informed of Bard’s promotional role to expand the RNF use into the “contraindicated” obese population. Rather, Bard told the FDA that it is the physician’s fault, not Bard’s, that filters were being incorrectly implanted in obese patients.

<sup>648</sup> FDA\_PRODUCTION\_00000048 at 00000180

in the sponsor's cover letter, "*it was determined that FDA would not accept an indication for limited retrieval (3-4 weeks) without clinical data; therefore, the sponsor now wishes to pursue market clearance of the modified design with an indication for permanent implant.*" Given the revisions in the indications for use, the sponsor requested that K050558 be converted from a Special 510(k) to a traditional 510(k).

521. Bard had agreed to drop its request for clearance as a G2 as a retrievable filter for a temporary indication. Ms. Smith thought Bard's marketing of a permanent filter still required submission of *in vivo* data to show that the proposed modifications of the G2 did not adversely affect the tissue of the IVC."

522. Regarding the FDA's request for the addition by Bard of a new black boxed warning, Ms. Smith wrote that she relied on Bard, making no reference to having her opinions confirmed the adequacy of Bard's labeling response with Bram Zuckerman, M.D. Director, Division of Cardiovascular Devices, a physician and cardiologist, or a member of CDRH's post-market staff familiar with review of the adequacy of a label to address post-market safety issue (underlining added for emphasis):

*The sponsor indicates in their response that the IFUs of other commercially available IVC Filters do not specifically address the safety and effectiveness of the device in any one patient population; therefore, the sponsor proposes alternate language as follows: There have been reports of complications, including death, associated with the use of the Recovery Filter System in morbidly obese patients," I find this statement to be acceptable as it adequately captures the information known to date regarding the implantation of the Recovery Filter System in morbidly obese patients. The sponsor had not added a warning regarding central venous lines as requested. The sponsor states that 'there is no bench-top testing or clinical evidence that shows that the Recovery Filter is susceptible to fracture or movement due to the use of central venous lines: I discussed the sponsor's response to this deficiency with Ms. Kennell and Dr. David Buckles, PVDB Branch Chief, to determine what information FDA would like to see in the labeling. At this time, it is unclear what evidence led FDA to request the proposed language; therefore, I find the sponsor's response acceptable.*<sup>649</sup>

**9. Bard, not FDA's reviewer, remained responsible for ensuring the adequacy of its own label, marketing, and commercial G2 filter performance.**

523. Despite Ms. Smith's unofficial opinion regarding her willingness to accept Bard's proposed label, Bard as the IVC filter expert—not Ms. Smith, a Chemist Reviewer or Ms. Kennel, a Microbiologist, both scientists without clinical training and experience—had the responsibility to ensure the adequacy of Bard's own label. Nothing prevented Bard from immediately accepting all of the FDA's proposed label requests including the use of a black boxed warning. Bard had not chosen to accept FDA's request. Bard, not Ms. Smith, should have been aware its own marketing

<sup>649</sup> FDA\_PRODUCTION\_00000048 at 0000182

actions had changed the intended use of the RNF (21 CFR § 801.4). Ms. Smith did not acknowledge that she was ever informed by Bard that its own off-label promotions encouraged physician to implant the RNF (and later G2) in morbidly obese patients for prophylactic placement prior to bariatric surgery.

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526. [REDACTED]

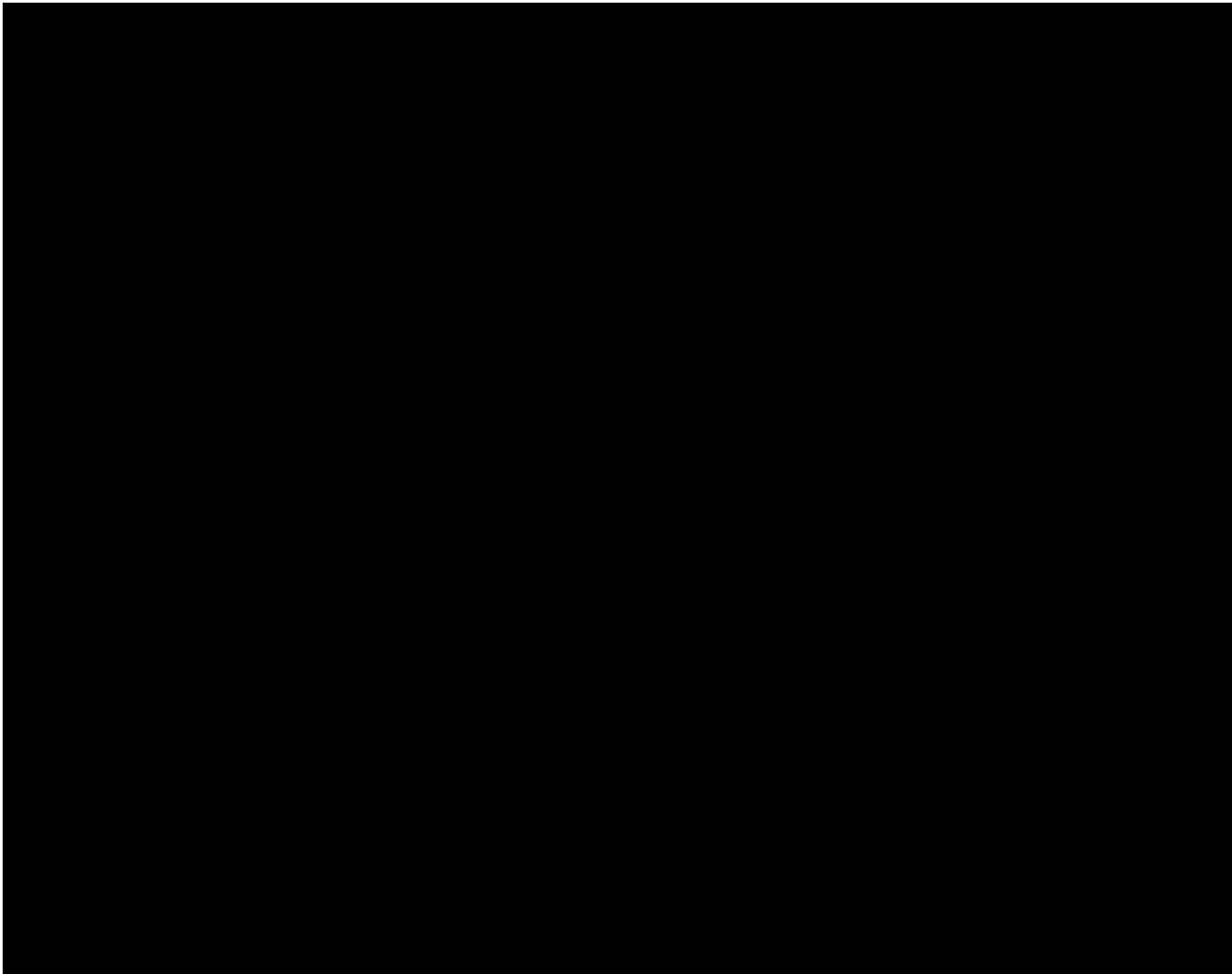
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<sup>650</sup> BPV-17-01-00142913

<sup>651</sup> BPV-17-01-00142913

<sup>652</sup> BPV-17-01-00142913

<sup>653</sup> BPV-17-01-00142913

<sup>654</sup> BPV-17-01-00046759

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(the SNF) that has virtually no complaints associated with it. Why shouldn't doctors be using it rather than the G2?<sup>673</sup>

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548. On October 31, 2007 Bard submitted a traditional 510(k) requesting FDA's clearance of retrievable indication for its Recovery G2 Filter (K073090)<sup>684</sup>. The device was the same as cleared in K052578 and K062887. The Bard's 510(k) request was not to change the filter but to change the IFU to add the "Optional Procedure" for Filter Removal and to delete the FDA's limitations of the prior 510(k) clearances prohibiting off-label use or Bard's promotion of the G2 as a retrievable filter. Nothing in Bard's G2 510(k) submission adequately informed the FDA's ODE reviewers that Bard was already actively engaged in marketing claims of improved performance (superiority) of the G2 Filter as a permanent filter when compared to the Recovery Filter. These claims had not been cleared based on FDA's 510(k) clearance of the G2 (Recovery Modification) as substantially equivalent to the RNF.

549. Bard obtained clinical data for G2 retrieval through its IDE Study EVEREST using RF-210F conducted for support of G2 retrieval.

**a. Bard's EVEREST clinical study ("Proof of Concept") supported FDA's clearance of a retrieval indication for the G2 filter.<sup>685</sup>**

550. The 510(k) clearance for G2 filter retrieval was supported by prior preclinical and animal testing submitted by the Bard in its G2 permanent filter 510(k)s. Bard now submitted the results of its EVEREST clinical study to support "retrieval" of the modified G2 filter. According to the NIH's Clinical Trials.gov website, EVEREST (Identifier NCT00556426) was first received from Bard on November 8, 2007 with the last update May 25, 2012.<sup>686</sup> EVEREST was a multicenter study, which enrolled 100 patients. The Principal Investigator (PI) was John Kaufman, M.D. Dotter Interventional Institute, OHSU Portland, OR. EVEREST had 11 investigators at 11 sites (1 investigator per site) with subjects enrolled between December 7, 2005 and July 24, 2006. Of the 100 patients enrolled, 91 completed the study, with 9 not completing (3 were withdrawn by the subject and 6 died). Patient enrollment was to include patients who were at temporary increased risk of PE requiring an IVC filter, and whom Recovery G2 Filter retrieval could reasonably be expected to occur within six months of device placement. There were 33 females and 67 males enrolled with the average patient age  $52.1 \pm 16.7$  years. Of the 100 patients, 43 had active thromboembolic disease, and 57 did not. All enrolled patients were to have a life expectancy of  $>6$  months. The cause of the six deaths in Everest were not described on the NIH website or in the EVEREST Abstract on Bard's webpage.<sup>687</sup>

551. Filter removal was attempted in 61 patients (61%), with successful removal in 58 patients (95.1% of those attempted). The three filter failed removals had tilting of the filter. With device tilting, the filter's tip became embedded in the vena cava wall preventing the Recovery Cone, forceps or snare from engaging with the filter apex so it could be removed percutaneously.<sup>688</sup> For

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<sup>684</sup> K073090 (BPV-15-01-00123629)

<sup>685</sup> Everest data would be published on the NIH's 'Clinicaltrial.gov' Website in November 2007

<sup>686</sup> <http://clinicaltrials.gov/ct2/show/record/NCT00556426?sect=X43ba9056>

<sup>687</sup> *Id.*

<sup>688</sup> M. Asch deposition, January 5, 2011, p. 101 L.9-19. The Asch Recovery study of 60 patients had an indwell time of 4 day-134 days, with the average 53 days.

the 58 filter retrieval patients, the length of time implanted in the patient was 140 days (range 5-300 days). Only 5 filters were retrieved after an indwell time in a patient greater than 210 days. The majority of filters (43/ (74%)) were retrieved after implantation in a patient of 90-210 days.

552. The percentage of patients with adverse events reported through 30-days post retrieval was 14.8%. For 76 adverse events, 6 (8%) were called serious (1 was discomfort associated with penetration, 2 reports of PE, 1 with caval stenosis, and 1 with DVT). Other adverse events recorded included: two patients with atrial fibrillation, one with atrial flutter, three with congestive heart failure, one with pericardial hemorrhage, one with pericardial effusion, three with gastric hemorrhage, one with retroperitoneal hematoma, one vena cava thrombosis, one vena caval injury; thirteen with DVT, three with PE.
553. The number of participants in the study analyzed for filter migration >2mm by imaging was 82 (58 retrieved, 22 non-retrieved reaching 6 months, and 2 non-retrieved subjects with attempted retrieval and imaging), with 12.2% showing caudal filter migration >2mm. There was one report in 83 patients of a fractured filter at 6-months (1%), and that filter was unable to be retrieved. Both filter migration (12.2%) and filter fracture (1%) occurred at 6-months, and according to the NIH's website, Bard classified these as "Safety Issues" for its G2 filter.
554. The FDA would accept Bard's EVEREST data as sufficient to support clearance of the "retrievability" of the G2 Filter. In fact, the EVEREST Study data actually supported the need for Bard to recommend that physicians promptly retrieve the G2 filter from patients when no longer clinically necessary or recommend to continue to monitor the status of the filter particularly with the reporting of onset of abdominal or chest pain or shortness of breath.

**b. Bard Posted the EVEREST abstract on its corporate website but with an inadequate and misleading description of its findings on filter risks.**

555. The EVEREST Study abstract was posted on Bard's Webpage as of May 25, 2014. It was titled: "Clinical Study Overview: The Bard Recovery G2 Filter Study (EVEREST)." The copyright date was 2008. There was no mention of migration >2mm occurring in 12.2% of the filters with unexpected increased movement caudally, or a fracture incidence of 1.2% in a patient unable to be retrieved, both considered as safety events in EVEREST by Bard. Unlike the NIH's website (2012), Bard's abstract on its corporate website listed only fifteen adverse events (15) which occurred in nine (9) study patients from retrieval through follow-up of 30-days post retrieval. Four (4) of the events were called serious (27%) with one event related to filter retrieval and the remaining three events attributed to intercurrent/pre-existing condition.
556. In contrast to the information on Bard's website, the final published abstract (2008) and the NIH's site (2014) both had 76 adverse events with six (6) (8%) called serious, including 1 patient with discomfort from caval penetration and another with caval stenosis. There was no mention of the six patient deaths listed on the NIH website or in Bard's website published abstract.

**c. Bard's Published EVEREST Study in 2009 Described "Unexpected" Caudal Movement**

557. The information from the EVEREST Study, after its use to support 510(k) clearance, would later be published in a peer-review journal in November 2009.<sup>689</sup> The 100 patients were enrolled between December 2005 and July 2006. The indications for filter placement were trauma (n=56), perioperative risk (n=16) and medical indications (n=28). The authors indicated that “Fifty-eight filters were placed prophylactically.” There was reportedly no difference in dwell times between successful and unsuccessful retrievals. The authors continued: “Although there were no cases of cranial migration, caudal migrations were observed in 12% of cases” (10 of 85 patients with complete data set). Other device-related complications described included (but are not included on the Bard’s posted 2008 abstract on its website): filter fracture (1/85, 1.2%), filter tilt of more than 15 degrees (15/85, 18%), and leg penetration (16/61, 26%). The recurrent PE rate was 2%, with no PE detected in the 30-day period of filter retrieval. The conclusion of the authors (2009) (also not on Bard’s corporate website or included in Bard’s G2 IFU or marketing- based on clinical data it had available for the G2 in 2006 before clearance for retrieval):

*Retrieval of the Recovery G2 filter was safe and successful in most patients. Caudal migration was observed as an unexpected phenomenon.*<sup>690</sup>

#### 4. Bard’s problems with the G2 filter continued after it was cleared for ‘retrieval’.

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<sup>689</sup> Binkert CA, Drooz AT, Caridi JG, Sands MJ, Kaufman JA, et al. Technical success and safety of retrieval of the G2 filter in a prospective, multicenter study, *J Vasc. Interv. Radiol.* Nov. 2009, 20(11), at 1449-53

<sup>690</sup> *Id.*

<sup>691</sup> *Id.*

<sup>692</sup> BPVE-01-00622862, Tessmer Exhibit 14

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Endovascular Snare Retrieval method to remove an IVC filter. There is Recovery Cone Removal System Retrieval with the cone fitting over the snare tip to withdraw the filter. However, the promotion goes on to make new and not cleared claims. For example claiming “atraumatic removal” based on the “elastic” hook design, then showing tissue without the hook (which is an empty space) but calling it a “sleeve” and extended dwell time. In terms of the EVEREST Study, the filter indwell time was up to 6 months for the G2, (a fact not being stated or recommended in promotions by Bard sales force). Also Everest showed an increased risk of tilting greater than 15degrees (18%) so it is not clear what Bard has supporting a new claim of “Self-Centering” for the G2 with a snare tip as the G2X:

#### ***EXTENDED DWELL TIME***

*Unique design of “elastic” hooks allow for atraumatic filter removal even after extended indwell times. Actual Masson’s Trichrome cross-section of the caval wall shows atraumatic removal of the filter. The with oval is the sleeve left behind after an “elastic” hook was removed.*

#### ***SELF-CENTERING***

*Specially designed pusher wire and articulated arms promote a centered filter placement, even though tortuous anatomy.*

566. The G2X Filter information did not warn physicians about the “unexplained” migration caudally (12%) seen in Everest (in 2006) for the G2 Filter, 1.2% fracture rate, 26% leg penetration, greater than 150 filter tilt of 18% at only a 6 months indwell time.<sup>695</sup> The risk for cephalad migration was still present with the G2X Filter.

567. G2 Marketing printed out on June 8, 2010 for the G2 Filter from Bard Peripheral Vascular website:

#### ***G2 FILTER SYSTEM***

*Indicated for Retrieval*

*Now with Option of Extended Retrieval, the G2 filter gives physicians complete control over their patient’s care.*

● ***Increased MIGRATION RESISTANCE***

● ***IMPROVED CENTERING***

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<sup>695</sup> Binkert CA, Drooz AT, Caridi JG, Sands MJ, Kaufman JA, et al., Technical success and safety of retrieval of the G2 filter in a prospective, multicenter study, J. Vasc. Interv. Radiol., Nov. 2009, 20(11), at 1449-53

● *Enhanced **FRACTURE RESISTANCE***

*\*Data on File*

*Secure Fixation*

*Easy to Use*

*Self-Centering*<sup>696</sup>

*Recovery G2 filter System: The Recovery G2 Filter combines the best design features of Bard's existing vena cava filters to create a brand-new filter platform- taking strength and stability to a new level.* <sup>697</sup>

568. Bard's marketing piece continued: "The newly enhanced Recovery G2 filter continues the Bard tradition of filter innovation spanning over a decade."<sup>698</sup>

569. Bard's marketing indicates to physicians the supporting information is available as 'data is on file.' This statement implies the information on file is available if requested by a physician. Mr. Carr was asked if Bard would provide results of testing to a physician if they requested to see it. He indicated that "no", it was considered confidential by Bard:

*Q. What about if a distraught physician wanted to know how the filter has been tested to see if it can resist fracture? Is he or she entitled to know that information?*

*A. No. it's confidential. No, not generally. It is confidential.*<sup>699</sup>

*Q. ...the distraught customer wants to know what is the official complication rate of the G2 filter compared to other filters. Is he or she entitled to have an answer to that question?*

*A. No. It's speculation.*

*Q. Why is it speculation?*

*A. Because I don't know the rates of other filters.*

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<sup>696</sup> BPV-17-01-00137620; BPV-17-01-00137622

<sup>697</sup> *Id.*

<sup>698</sup> BPV-17-01-00137588

<sup>699</sup> Carr deposition 4/17/2013, p. 162, L. 19-24

*Q. Would Bard at least provide this distraught customer, this physician, with its official complication rate of the G2 as of August 2008?*

*A. No. It's confidential information.*<sup>700</sup>

[REDACTED]

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differences in risks for its G2 IVC filter design when compared to the original Recovery IVC. The risks reported for the G2 IVC filter design were greater for caudal migration, tilt, fracture, perforation than the older RNF.<sup>705</sup>

572. Bard would market a device called its G2Express Filter System only from July 2008 through November 2009. According to Bard's Concept POA "G2 Platinum Concept POA" authored by Bret Baird, dated May 5, 2009, in 2008, Bard, at that time the current leader in optional IVC Filters in the United States, selling its G2/G2X IVC family had the primary IVC market share (23%)).<sup>706</sup> Bard made an internal decision to stop sales of its G2Express Filter System in the later part of 2008 (It was 510(k) cleared by FDA in 2008). Hospitals and Bard's sales force were officially informed of Bard's discontinuation of the "G2Express IVC Filter System" by a later April 2009 letter. <sup>707</sup> The market withdrawal, as with the RNF was not classified a recall by Bard or linked to a safety issue for the product. There was no mention by Bard of a need for notification of the FDA of the reasons for the G2Express product discontinuation.

573. Bard's subsequently marketed a new and improved "G2X" IVC filter while continuing to use the same G2Express IVC filter platform. The prior G2 Express filter name was changed by Bard's marketing plan to its new G2X IVC Filter. Both devices shared the same product code for product identification and ordering. However, Bard beginning in January 2009 Bard marketed its G2X Filter to physicians calling it the "new IVC filter system." Marketing of the G2X began January 2009 and extended through April 2010. It appears applicable to a Special 510(k) cleared on October 2008 for design modifications to the delivery system for Bard's G2Express Filter. There is no reference to any market withdrawal or recall of the G2Express Filter or its delivery system from the Field or hospitals. The G2X implanted the same G2Express IVC filter and only differed with a new delivery system. <sup>708</sup>

574. In 2009 there is a Bard presentation titled "G2 Platinum" with the following two PowerPoint slides. The first slide discussed tilt and its association with IVC penetration and adjacent structures based on the angle of the tilt. Bard next had "tilted filters are subjected to loading conditions they were not designed to withstand, which may lead to fractures." The slide finally addressed the Fishbone analysis with "insufficient caudal anchoring as the possible root cause of caudal tilts and migrations, and indirectly penetrations and fractures."<sup>709</sup>

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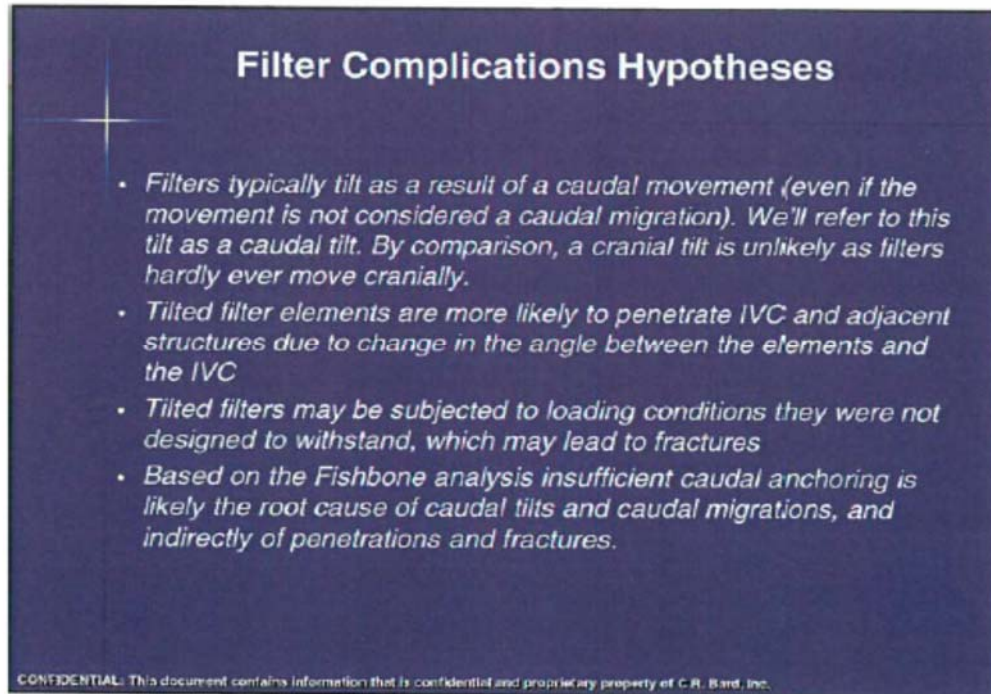
<sup>705</sup> Becket Exhibit 9

<sup>706</sup> Modra Exhibit 7, BPVE-01-00597792

<sup>707</sup> Modra Exhibit 4

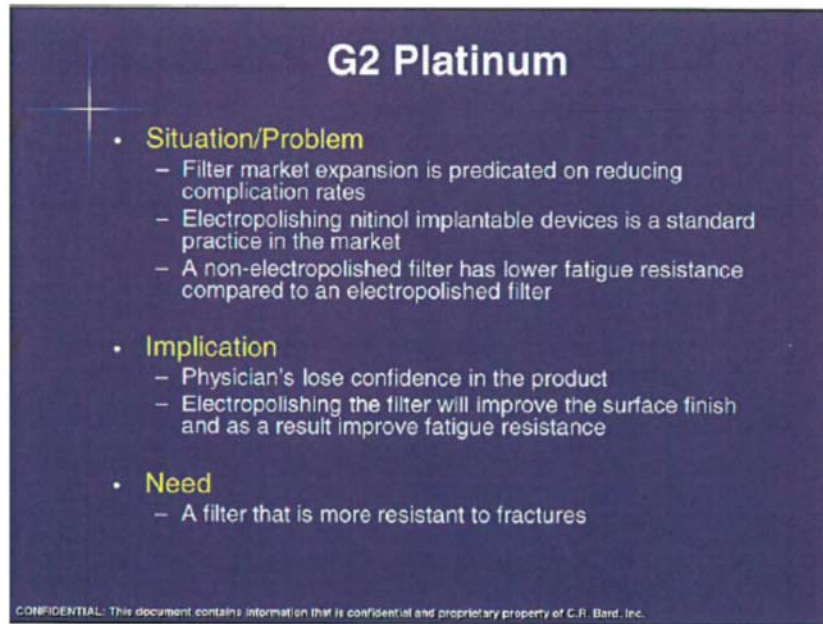
<sup>708</sup> Modra Exhibit 8

<sup>709</sup>



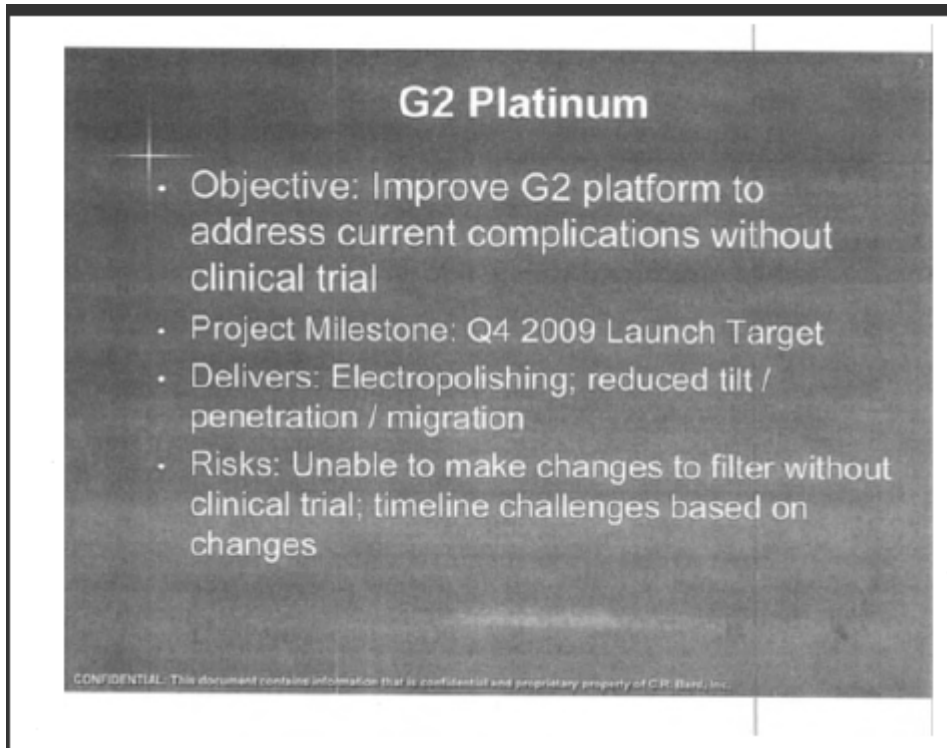
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575. The next slide is titled “G2 Platinum” and simply states that “electropolishing nitinol implantable devices is a standard practice in the market” also Bard is aware in 2009 that “a non-electropolished filter has lower fatigue resistance compared to an electropolished filter.” The implication of filter fractures has nothing to do with ensuring or addressing patient safety, but rather “physician’s lose confidence in the product.”



711

576. Bard had a meeting “to analyze EVEREST and MAUDE data and provide justifications for proposed changes to G2 filter” and “the new improved filter platform (G2 Platinum).” Slide 3 of the presentation states:



712

<sup>711</sup> BPVE-01-00665789

<sup>712</sup> Ganser Exhibit 534

577. This internal Bard document repeats the need in 2008 for Bard to make design changes to the existing G2/G2X device to help resolve problems for physicians related to filter fracture, tilt, penetration and migration.

578. Included on the G2 Platinum slide above, as an 'Objective' is the statement: "Improve G2 platform to address current complications without clinical trial." The same objective is now retranslated into a risk that Bard will be unable to make electropolishing changes to the filter without conducting a clinical trial.

579. Bard has placed the conducting of a clinical trial as if only to respond to the FDA. Responsibility for ensuring the adequacy of final filter design rests with Bard and not the FDA. It is the duty of Bard to ensure the safety, efficacy of its filters including the adequacy of the proposed changes to a final product finished product to ensure it can continue to perform as intended when permanently implanted in the body's vascular environment. The capability of performing clinical trials has been designed by Congress to facilitate a sponsor's path to marketing a product cleared by 510(k) by obtaining human performance data ethically. When an implanted device has been cleared by 510(k), it is the duty of the sponsor to make sure it performs as described to FDA in the 510(k). When a device like RNF and then G2 with a shared filter platform both fails to perform as cleared for marketing, showing unacceptable risks as reports of clinically significant migrations, fractures, tilts and perforations, then a clinical trial is one of the best options available to a sponsor like Bard to ethically and scientifically identify the changes necessary to market a successful IVCF. The clinical trial would also be able to show if a proposed corrective fix is not feasible with the current filter design.<sup>713</sup> Essentially a clinical trial should not be an objective and risk to be avoided for a manufacturer intending to market a safe and effective IVCF.

580. Mr. Carr was asked about Bard's lack of actions to notify physicians caring for implanted patients with the G2/G2Express/G2X filters to communicate potential risks and need for monitoring of patients with filters:

*Q. Have there been any Dear Doctor letters of informational documents provided to physicians regarding the issue of medical monitoring of patients that have the Recovery filter, the G2, or the G2 Express?*

*A. I don't believe so.*<sup>714</sup>

Mr. Carr was asked in Bard had studied the performance and survival of filters implanted in patients beyond the 300-days of the Everest study.

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<sup>713</sup>Ganser Exhibit 534

<sup>714</sup> Carr deposition 4/17/2013, p. 146, L. 11-15

*Q. Bard has not studied clinically in humans the risk of caudal migration, fracture, tilt, or penetration beyond the 300-day Everest study. Is that a correct statement?*

*A. Again, yes, it is.*<sup>715</sup>

**C. BARD'S G2 PLATINUM FILTER WAS RENAMED "*ECLIPSE*" TO BRING OUT A NEW PRODUCT, ADDRESS LUKEWARM SALES AND WANING PHYSICIAN SUPPORT**

**1. Bard's Product Opportunity Appraisal for the G2 Platinum Filter, Project #8088**

581. The Eclipse had a CONCEPT POA dated May 5, 2009 for Bard's "G2 Platinum IVC Filter Development", Project No. #8088.<sup>716</sup> The author of the POA was Bret Baird.<sup>717</sup> The Concept POA described an opportunity to improve the G2X platform. It was not intended to introduce a "new filter platform design", but rather to improve the current G2X filter and modify the femoral delivery system. The G2 Platinum was to be an electropolished IVC filter that could be deployed femoral, jugular/subclavian. The G2 Platinum would have a modified femoral delivery system. The reason that interventional radiologists, vascular surgeons and cardiologists would think the product is the "improved surface finish that is "*consistent with emerging industry standards*", as well as the long-term retrievability, caval centering, dual-level filtration and multiple retrieval options.<sup>718</sup>

582. Bard's description of the "**Unmet Needs**":

1) **The Situation:** Electropolishing Nitinol implantable devices is a standard practice; ISO standards for filters could potentially require corrosion testing per ASTM-F2129 in the future; some physicians are retrieving the filter off-label using "bronchial forceps" to pull a tilted filter off of the vena caval wall. Therefore, for Bard to implement surface finishing for the G2 filter to market the Eclipse (G2 Platinum), Bard Engineering had only to introduce already established and standard industrial practices for production of its Nitinol device. There was no new research required for Bard to start electropolishing its filters. The research Bard should have conducting to support its marketing claims would have been to look at the effects (positive and negative) of adding electropolishing to manufacture of its IVC filter. Such testing could have been done by Bard's scientist as animal or bench testing. At any time, Bard also could have conducted a study in changes in filter performance with prolonged implantation in patients, prospective or retrospective.

2) **The Problem:** Bard filters are not currently electropolished; bronchial forceps can apply a significant force on the snare hook or the filter during removal. The problem was that the

<sup>715</sup> Carr deposition 4/17/2013, p. 153-4, L. 25-4

<sup>716</sup> Modra 7, BPVE-01-00597792

<sup>717</sup> Modra 7, BPVE-01-00597792

<sup>718</sup> Modra 7, BPVE-01-00597792

snare was breaking when physicians were attempting to retrieve the filter, particularly with a difficult retrieval. This visible complication would have immediately been associated with physician perception about an overall quality issue with the device, particularly when having to use the force of biopsy forceps to pull on and retrieve the filter from a patient.

3) **The Implications:** Current Bard filter customers are without the advantages of electropolishing- smoother and more passive surface finish will: *“improved fatigue and corrosion resistance”*; too much force applied to the snare hook can break it off. Again, the implication is that physicians would begin to question the quality and performance of Bard’s retrievable filter and consider using alternative filters.

4) **Needs:** A filter that meets today’s standard of practice in surface finishing processing; an enhanced G2X filter with *“improved fatigue and corrosion resistance; improved retrieval hook.”*

5) **Critical Success Factors:** The G2 Platinum electropolished filter must provide equivalent or improved performance compared to the G2X filter and not introduce additional complications. The G2 Platinum must actually be an improvement for a customer.

6) **Voice of the Customer Plan:** User input was obtained for this project utilizing a variety of means including: filter placement observations; primary qualitative research, BPV sales team input, BPV complaint history, MAUDE and FDA website searches; Bard and IMS sales; Clinical literature and text book. The complete customer inputs are in Design Input Summary (DIS-8088).<sup>719</sup> The DIS-for Platinum was June 23, 2008 Project #8049.

583. There had been a pre-IDE discussion with the FDA on March 18, 2009. It was thought that the project did not require Bard to conduct a clinical trial.

584. Bard’s “Intended Claims for Marketing of the Eclipse Filter”:

- *The G2 Platinum filter offers a smoother, more passive, surface finish yielding improved fatigue resistance*

- *A New improved retrieval hook further protects against hook failure*

- *The G2 Platinum filter offers a more robust design.*<sup>720</sup>

585. The positioning of the G2 Platinum filter would be promoted as a “new Bard filter.” It will be positioned as an “enhanced” Bard filter that continues the long-term retrievability, dual-level filtration, caval centering and multiple retrieval modalities. *“The message to our customer base is one of continued improvements.”* The POA continued with the plan to rebrand this Bard IVC filter, number it as a 500 series (G2 (300 series in the US), G2X (400 series in the US) and imply it is a new filter despite it still being the same as the Bard G2X filter:

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<sup>719</sup> Modra 7, BPVE-01-00597792

<sup>720</sup> Modra 7, BPVE-01-00597792

*We will take the opportunity to rebrand the filter with this launch. We will promote it with a new name, new packaging, and new product codes.*

*With the launch of the G2 Platinum filter we will begin to phase out the G2 and G2X filters. These filters will phase out over a 6-month period in the US... We will significantly raise the price of the G2 and G2X at time of launch to help motivate customers to move over to the Platinum Filter.*

### **Call Points**

*The primary call points are current and new filter customers, both domestic and international including interventional radiologist, interventional cardiologists and vascular surgeons.<sup>721</sup>*

586. At the time of the POA, BPV with the G2/G2X had 23% of the IVC filter market share in 2008, the primary optional IVC filter share (compared to Cordis with 25% as permanent IVC Filter share with TrapEase- \$1060). Bard sold the most expensive filter (\$1273) and had the primary share of the optional filter market.<sup>722</sup>

587. As discussed above, for the G2X Filter, Bard internally decided it would discontinue all sales of its G2X IVC Filter System in May 2009<sup>723</sup>. However, its sales force and hospitals were not officially informed of the G2X discontinuation from Bard's catalog until one year later on April 2010<sup>724</sup>, shortly after Bard's launch of its 'rebranded (renamed)' "G2 X IVC" filter. The rebranded IVC filter (internally called the 'G2 Platinum IVC Filter' as well as the Vail Filter) would be sold commercially only in the United States and only using the name 'Eclipse IVC Filter System.'<sup>725</sup>

588. On October 27, 2009 Bruce MacMore issued a memorandum to the 'Vail Transfer Fact Book', Subject: Vail Transfer- Scope Statement.<sup>726</sup> The memo described the specifics of the manufacturing of Bard's Vail Filter as the Eclipse. According to Mr. MacMore, the primary difference for the Vail project compared to the marketed G2X Filter was that Bard contracted with an outside vendor to electropolish the wires before filter assembly and "additional machining and handling of the device" allowing the potential benefits of surface finishing to be reduced. The device specifications, delivery system, manufacturing facility, manufacturing equipment and personnel making the Vail filter were all the same as the G2X. Despite the significant issues for the G2X and Vail remaining the same, including the specifications, Bard's introduction of the new Vail Filter would appear based on its new name, packaging, and addition of a new color to

<sup>721</sup> Modra 7, BPVE-01-00597792

<sup>722</sup> *Id.*

<sup>723</sup> Concept POA G2 Platinum IVC Filters Development May 5, 2009 Prepared by Bret Baird, Modra Exhibit 7, BPVE-01-00597792

<sup>724</sup> Modra Exhibit 6; BPVE-01-00761124

<sup>725</sup> Modra Exhibit 7, BPVE-01-00597792

<sup>726</sup> BPV-17-01-00145634

the delivery system, to be a new product series with the new identifier (RF-500 F/J) reinforced by Bard's marketing and enhancement claims. Bard's 'concern and commitment to product innovation' for customers had actually developed a new and "enhanced" IVC Filter system that appeared to preform differently from the flawed G2/G2X Filters.<sup>727</sup> The proposed launch date for the Vail Filter was January 2010.

589. Mr. MacMore continued to summarize the minimal changes of the Vail Filter when compared to the G2X Filter already produced at GFO:

*No new equipment is required as the old product will utilize all the current equipment and processes. The electropolishing of the wires will be performed by an outside vendor and the component will be shipped to GFO for assembly. New fixtures (jigs) will be used to build Vail filters.*

*The Vail product will phase out the current G2X with similar volumes of production. Specifications for the G2X will remain in place to allow for additional production if required.*

*RF500J- Jugular Delivery System*

*RF500F- Femoral Delivery System*

*RF700J- Jugular Delivery Systems (international)*

*RF700F- Femoral Delivery System (international)*<sup>728</sup>

## **2. Bard Submitted a Special 510(k) Requesting to Market Its Eclipse IVC Filter System in the United States**

590. On November 25, 2009, Bard submitted a new Special 510(k) for marketing a filter system named the Eclipse Filter System- Femoral Delivery Kit, Eclipse Filter System-Jugular/Subclavian Delivery Kit Model RF-500F Model RF5 (K093659).<sup>729</sup>

591. The Special 510(k) for the Eclipse would be cleared on January 14, 2010. The G2 Express Filter System (K082305, cleared October 31, 2008) was the cited predicate for the Eclipse. The FDA was told that the Eclipse "was an improvement of the surface finish of the filter raw material wire by electropolishing the wire prior to forming the filter."

592. As with the G2 Express, which introduced a new snare tip for the filter, reportedly the Eclipse still consisted of twelve Nitinol wires emanating from a central Nitinol filter hook. As with Bard's Recovery and G2 Filters, the Eclipse filter provided two levels for embolic filtration: the

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<sup>727</sup> BPV-17-01-00145634

<sup>728</sup> BPV-17-01-00145634

<sup>729</sup> BPV-17-01-00116991 to BPV-17-01-00117153.

legs (lower level) and the arms (upper level). The Eclipse, unlike the G2 Express or the Recovery Filters was marketed with claims of benefits (superiority) based on electropolishing (surface finishing) of the 12 Nitinol wires, as well as the hook, before final assembly into the filter. As with Bard's Recovery and G2 Filters, the Eclipse was intended to be implanted in patient with IVC diameters less than 28mm. The indications for use remained exactly the same as the Recovery and G2 Express predicates as a permanent filter for prevention of PE with an IFU which included an Optional Procedure for Filter removal. There was no clearance by FDA for "prophylactic use" or use in morbidly obese patients or patients undergoing elective bariatric or orthopedic surgery. There was no clearance with a recommendation when the device should be removed from a patient when no longer clinically indicated to prevent PE.

593. Bard submitted a Special 510(k) for the Eclipse Filter Systems- Femoral and Jugular/Subclavian Delivery Kits on May 21, 2010 which was cleared June 25, 2010 (K101431). The predicate cited was Bard's prior Eclipse Filter System (K093659, cleared January 14, 2010). The modification to the Eclipse System was to add a Patient Brochure and an Implant Card in the device labeling to be held in a special pouch.

594. FDA requested that Bard remove a statement that there was "*no established timeframe for removal of the filter*" from the label.<sup>730</sup>

595. The Eclipse IVC System would be sold to physicians and hospitals as Bard's new electropolished G2X filter (G2 Platinum). However, Bard had already obtained FDA's clearance to electropolish the surface of its G2 filters.<sup>731</sup> Use of a new product name, despite its similarity to the prior G2/G2Express filter products, was reportedly Bard's attempt to address the lukewarm sales enthusiasm by its own sales force to market its G2/G2X IVC filters.<sup>732</sup>

596. Bard's sales force was instructed to begin to take orders for Bard's new Eclipse IVC Filter System shortly after FDA's January 14, 2010 510(k) clearance (see 510(k) discussion below). Bard's Sales force would start carrying the new Eclipse IVC Filter Systems as trunk stock for physicians to try in February 2010 (before it announced April 2010 discontinuation of the G2X). Reportedly, the Eclipse IVC Filter was marketed only in the United States, with the trade names "G2/G2X" continuing to be used by Bard for the filters internationally. The initial G2 Filter System (pre-snare/hook) would continue to be marketed by Bard until finally discontinued in December 2011.

597. Only United States physicians would hear Bard's new performance claims for its Eclipse IVC Filter. The Eclipse Filter claims revolved around Bard's introduction of a standard medical

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<sup>730</sup> K101431 BPV-17-01-00171679 (Source: Dr. Tillman's Expert Report, p 58)

<sup>731</sup> The original G2 IVC filter (without the snare retrieval hook) would continue to remain marketed by Bard in the United States until December 2011. Outside the United States, both the G2 and G2X IVC filters would both continue to remain commercially available. Modra Exhibit 4

<sup>732</sup> Carr deposition 4/17/2013, p. 108-9, L. 22-22; p. 127, L. 9-14; p. 137, L. 6-10

device surface finishing process to manufacturing. The change in device finishing reportedly produced a more robust snare hook to use for retrieval and could help improve filter performance.

598. Bard's United States business plan in 2010 for its G2 IVC filters was to deplete all remaining United States inventories of G2X Filter Systems by the end of the 12-week Eclipse launch period. The Eclipse Filter, continuing the same G2X IVC filter design, could continue to use the same G2X femoral and jugular delivery systems. The earlier G2/G2X IVC Filter products would continue to remain available only short-term.<sup>733</sup> To help encourage quicker adoption of the rebranded Eclipse IVC Filter (G2/X IVC Platinum filter) by physicians and hospitals in the United States, Bard significantly increased the cost of its remaining G2 and G2X Filter Systems. The 2010 Eclipse System, with the G2X filter platform, surface finishing, and same delivery system, despite the similarities to the G2X filters, was marketed by Bard's sales force to physicians with new claims of a smoother, more passive 'electropolished' filter surface able to yield improved fatigue resistance (performance) and offering a new improved retrieval hook.<sup>734</sup>

599. Bard's development of the Eclipse IVC System, despite its marketing claims and promotions made only to United States physicians, was not supported by Bard's conducting clinical studies or scientific research studies or testing to validate and support new Eclipse marketing claims of enhanced performance or improved retrievability with the hook.<sup>735</sup> Bard utilized the opportunity of introduction of its Eclipse IVC Filter rebranding of the G2X as a new marketing opportunity to sell its established G2X filter platform while conveying to its customers a message of Bard's IVC filter commitment to "*continued improvement*."<sup>736</sup>

The Special 510(k) for the Eclipse was substantially equivalent to the predicate G2Express with the primary change made to the trade name for purposes of marketing.

### **3. The Eclipse and surface treatment-electropolishing.**

600. One of the proposed changes for the marketed Eclipse filter was the addition of a new surface processing step called electropolishing. On May 31, 2007, Bard's Mike Randall sent Arun Agrawal, Ph.D, Senior Project Manager of CC Technologies, Inc. at DNV, Dublin, OH ten (10) packaged SNF for CC to conduct corrosion testing using ASTM F2129-06. On June 12, 2007, Mr. Randall sent an email to Dr. Agrawal at CC Technologies "Subject: SNF Filter Test Stoppage" requesting him to not test Bard's SNF samples for corrosion.<sup>737</sup>

601. There is a December 7, 2007 report sent to Mike Randall, BPV titled "Corrosion Testing of Set 4 Vena Cava Filters (Project No.:81174891) from CC Technologies. Earlier, in October 2007 Bard

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<sup>733</sup> Modra Exhibit 5 BPVE-01-00596766

<sup>734</sup> Modra Exhibit 7, BPVE-01-00597792

<sup>735</sup> Bard's internal PowerPoint "Tetra Project #8049-Concept Design Review September 5, 2007." Janet Hudnall's PowerPoint Presentation titled "Design Input Summary" listed Bard's "Design Input Sources": market research; expert panels; field visits & clinical interviews; clinical literature review; complaint review; MAUDE website review; regulation review. No listing of Bard sources of design as clinical trials or scientific research and testing.

<sup>736</sup> Modra Exhibit 7, BPVE-01-00597792

<sup>737</sup> BPVE-01-01349522

had sent a set of Nitinol filters for corrosion testing. The objective was for CC Technologies at DNV to evaluate the corrosion susceptibility of the test filters using the cyclic potentiodynamic polarization (CPP) test technique per ASTM F2129-06.

602. The goal of ASTM F2129-06 testing was to generate a CPP curve as a plot of electrode potential vs. current density on a semi-logarithmic scale.

603. Bard was not seeking the CPP value of the ASTM test. But, rather Bard wanted to derive two parameters about the corrosion potential of the surface. The parameters were the derived  $E_{bm}$  (See Figure 1) and  $E_{pm}$ , which are not part of the ASTM Standard's values.

604.  $E_{bm}$  is a measure of the 'breakdown or pitting margin' and  $E_{pm}$  'pitting protection margin'. The larger the  $E_{bm}$  value measured, the greater the resistance of the metal device surface to localized forms of corrosion in the test environment (for example pitting). The higher the value for  $E_{pm}$  the greater the ease of repassivation (return back to the original surface state) (rebound/repair/survival/biocompatibility) of the device after exposure to localized breakdown.

605. Per Bard's request the following six filter groups were tested: Group A, Group C, Group D, Group B, Group E and Group F. According to the pictures of the surfaces, Group A -had severe pitting and a broken arm (fracture); Group B- severe pitting; Group C- incidental pits; Group D- no apparent pitting; Group E- severe pitting, and Group F- severe pitting. Of the photographs of received and tested filters, only Group E and F filter contained an upper retrieval hook like a G2Express/ G2X/Eclipse filter.

606. For the filter groups that experienced pitting (Groups A, B, C, E and F) none of the groups yielded  $E_{pm} > 0.200$  mV for each of the three filters tested in the group. In terms of the acceptable minimum pitting protection margin for the metal Nitinol implant, the occurrence of surface pitting significantly altered  $E_{pm}$  to be measured below the acceptable minimum surface value (underlining added for emphasis):

*Similarly, a high value of  $E_{pm}$  implies a relative ease of repassivation following localized breakdown of the specimen. In general, a value of 200mV for the  $E_{pm}$  is considered a minimum for practical use of the specimen in the service environment that was simulated by the test solution.<sup>738</sup>*

- Group A- lowest  $E_{bm}$ =.353V severe pitting damage;
- Group B lowest  $E_{bm}$ =0.402 V severe pitting damage;
- Group C lowest  $E_{bm}$ =.599 V- suffered incipient pits, but did not repassivate;
- Group D no evidence of passivity breakdown and no pitting;
- Group E, lowest  $E_{bm}$ =0.336V severe pitting damage;
- Group F lowest  $E_{bm}$ =0.306 V severe pitting damage.<sup>739</sup>

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<sup>738</sup> BPV-17-01-00180307

<sup>739</sup> *Id.*

607. The ASTM F2129-06 parameters derived by Bard showed the potential effects of pitting (corrosion) of the Nitinol metal filter following long-term product survival (repassivation). Group D showed the best surface properties and long-term performance of the six groups with no evidence of passivity breakdown. Group D was a G2 filter with both ‘electropolishing + passivation treatment.’ Both the EP and passivation treatment were required to protect a Nitinol metal implant from passivity breakdown and pitting (corrosion) by ASTM F2129-06.

**4. Bard’s Eclipse design specification, unlike G2 filter, required migration resistance better than a Recovery filter Based on clinical experience.**

608. Under Bard’s Engineering Rationale for Eclipse, the specification stated: (1) Migration resistance must be better than Recovery Filter based on clinical experience (Reference is FDA’s MAUDE database); and (2) the assumption that clinically the maximum blood pressure gradient observed in an occluded IVC is less than 50 mmHg (Reference RD-SOP-035.03, IVC Filter Migration Resistance Study and RD-SOP-050.00 In-Vivo Occlusion Migration Resistance and Deployment/Recovery Study (NMT Documents). There was no longer any mention to migration resistance similar or greater than the SNF. The clinical experience was the FDA’s adverse event database, not Bard’s own internal complaint files and testing. The FDA’s MAUDE database is known for its under-reporting since it is a passive database without FDA’s verification of the information. It can be sued to examine reporting for trends. Unlike the FDA’s database, Bard could have chosen to use its own complaint database and/or testing, with information for Recovery and Eclipse which could be verified and would have a denominator.

609. On November 16, 2009, Gin Schultz emailed two documents to Gary Dolch. One of the documents was titled “Nicholson Talking Points.” It stated that “Other Data Points from Dr. Nicholson-77 of the 189 patients agreed to participate in a follow-up fluoroscopy. 28 had a RNF and 49 a G2 filter. They found that 7/28 (25%) RNF had fractures, with 5 of the fractures called symptomatic. For 6/49 (12%) of the G2 filter patients had fractures, but none were symptomatic. Bard’s Communications Option for the Nicholson data-“Engage Scott Treotola for rebuttal (he is writing a paper on benign filter complications.).”<sup>740</sup>

610. A late 2009 report was titled “Idea POA Eclipse Anchor Filter (Revision 0) stated in the summary that the POA described the addition of caudal anchors to the next generation (post G2/G2X) Eclipse Filter. Before Bard could market its next generation Eclipse (G2 Platinum) filter, it was already discussing a future addition of new caudal anchors to the legs. This Eclipse device with caudal anchors would later be cleared and sold as renamed Meridian Filter. The rationale for the new anchors for the Eclipse was “feedback from customers, the field and our own clinical data have shown an increased frequency of migration in the caudal direction with the G2 and G2X filters as compared to the Recovery.” Bard continued in 2009 that “The application of caudal anchors would potentially eliminate the failure mode and reduce tilting of the filter.”<sup>741</sup>

*Value Proposition*

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<sup>740</sup> BPVEFILTER-01-00203546 (Nicholson talking points)

<sup>741</sup> BPVE-01-02077858

*The Eclipse Anchor Filter will retain the advantage of the G2/G2X /Eclipse including the retrievable indication while improving caudal migration resistance. This improvement in caudal migration resistance should reduce subsequent tilt, fracture, and penetration.*

*Physicians will buy this filter because of long term retrievability, dual level filtration, multiple retrieval options, and centering capabilities as well as improved stability within the vena cava as compared to the G2, G2X and Eclipse.<sup>742</sup>*

611. The Eclipse with caudal anchors in the 2009 ‘Idea POA’ was already being positioned by Bard as its “premier optional filter” for existing and new Bard customers. The new caudally anchored Eclipse filter was intended to:

*...infuse enthusiasm for the product into the sales team, and address the quality issues with predicate filter products. The performance issues of the BPV optional filters have led to sales attrition and these complications overshadow the unique long-term retrievability of these products. These experiences have created a lukewarm opinion of the product with the sales team and resulted in lost business opportunities. This project should not only reduce physical complications but should also help to address psychological reservations both in the sales team and with customers regarding BPV optional filters.<sup>743</sup>*

## **5. Bard Launched the Eclipse Filter System in the United States in January 2010.**

612. The launch of the Eclipse Filters occurred in the United States at the 2010 National Sales meeting on January 14 and full market release occurred the following Wednesday on January 20, 2010. The enhancement of the surface finish was well-received as seen in the transition from the G2X to Eclipse. The original objective was to phase out both the G2 and the G2X. “Since G2X was the immediate predicate to the Eclipse the objective was to phase it out quickly followed by G2.”<sup>744</sup> According to the chart, by April 2010 G2X unit sales were only 12% of overall Bard optional sales, and by June the product was completely phased out. It was decided by the team and management to make the phase out of G2 longer.
613. Some of the Bard sales managers indicated that the lack of concrete data showing improvements with the enhancement of the surface finish made it less effective. In terms of sales, the Eclipse sales were under the target numbers of 2010. Internally, Bard employees speculated that this was due to legal promotional activities against filters, as well as some negative clinical studies that were published. “Most recently, Dr. Nicholson published his recent experience with Recovery filters in a retrospective report that included a high record of fractures.”<sup>745</sup>

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<sup>742</sup> BPVE-01-02077858

<sup>743</sup> BPVE-01-02077858

<sup>744</sup> BPV-17-01-00170358

<sup>745</sup> BPV-17-01-00170358

614.A Bard internal document, dated April 27, 2010 stated:

*The Eclipse launch introduced a product that addressed a shortcoming with its predecessors G2X and G2 through electropolishing. The change in brand name and codes was to create a break with the baggage associated with the previous versions despite the fact that the new iteration was the same as G2X in every way but one.*<sup>746</sup>

615. The same April 27, 2010 Bard memorandum, approximately three months after launch of the Eclipse referenced the release of Bard's "Eclipse Anchor Filter" that would be designed to improve "caudal migration resistance," and "*reduce subsequent tilt, fracture and penetration.*" As discussed above, Bard had been engaged in development of the caudally anchored Eclipse as a premium Eclipse IVC filter since the 2009 to address the risk of caudal migration. Yet, Bard launched the Eclipse product without caudal anchors in January 2010. The Eclipse without caudal anchors stayed on the United States market until sometime in 2011, without the changes to address reducing caudal migration, reduction in tilt or penetrations.

616. The February 2017 Expert report of Dr. Rebecca Betensky as relates to her analyses of Eclipse complaint/AE data states:

*As of **July 31, 2010**, there were statistically significant increased reporting risk ratios for **migration** (RRR = 20,  $p = 0.022$ ), and **caval perforation** (RRR = 5,  $p = 0.017$ ) for the **Eclipse** compared to the SNF. A marginally statistically significant increased reporting risk ratio was maintained for **caval perforation** (RRR = 4,  $p = 0.056$ ) even after assuming that there were 5 additional adverse event reports associated with the SNF.*

*As of **May, 2011**, there was a statistically significant increased reporting risk ratio for **filter fracture** (RRR 3.6,  $p = 0.005$ ) for the **Eclipse** compared to the SNF.*

*As of **December, 2011**, there were statistically significant increased reporting risk ratios for **filter fracture** (RRR 2.9,  $p = 0.0003$ ) for the **Eclipse** compared to the SNF. These RRR's increased through 2012 (4.5), 2013 (5.3), and 2014 (5.8) with similar  $p$ -values  $< 0.0001$ ."*

617. The Eclipse device was subsequently replaced by Bard's Meridian filter system (Eclipse with caudal anchors) in August 2011.

618. It is my opinion that the piecemeal changes for Bard's development and release of the Eclipse IVC Filter system in the United States continued Bard's inadequate response to complications and risks reported for the G2/G2X filters, and just as occurred with the flawed RNF, G2 and G2X members of the Recovery Family of IVC Filters, the Eclipse should not have been marketed by

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<sup>746</sup> BPVE-01-00580608-609

Bard as represented to its sales force and physicians as a significant improvement in Bard's permanent and retrievable filter platform.

619. With Bard's launch of each new member of the Recovery Filter Family, beginning with RNF and extending through the Eclipse, it would have been the expectation of physicians that Bard, as a responsible United States medical device manufacturer would have taken the necessary steps and actions for design and testing and as required by 21 CFR 820 as part of Quality Systems to develop and sell a safe, effective and adequately labeled IVC filter. The Bard documents do not support that Bard's actions developing and selling the Recovery Family of Filters adhered to accepted methods for quality product development and commercial oversight.

**D. The Meridian: a next generation Eclipse filter with caudal anchors.**

620. Bard claimed that the Meridian: The Meridian Filter benefitted the patient due to the high clot capturing efficacy (RBA-0003) and caval patency. In addition, since the Meridian filter is similar to the Eclipse, G2X, and G2 in design, the clinical history of the G2 has been summarized in 510(k) Submission K073090. Furthermore, the G2 filter offers the option for retrieval after an extended period of time. Based on the clinical history of the G2 Filter, *"which outlines many successful uses and benefits to the patient, it can be concluded that the overall residual design and manufacturing risks are tolerable and acceptable."*<sup>747</sup>

621. The Meridian is essentially the same electropolished filter as the Eclipse but with added caudal anchors to the arms. The Meridian has features shared with the entire RNF family of retrievable filters but now includes added downward pointing caudal anchors of titanium (Ti-Al-4V-Eli) laser welded onto the arms of an Eclipse Filter. The anchors were added to help accommodate a broad vena cava diameter range, with placement of two types of anchors added to alternating arms of the filter. Like all the Eclipse, the Meridian is made of twelve shape-memory (Nitinol) wires emanating from a central snareable tip. The twelve wires form two levels of filtration (arms, legs) all pointing downwards. The filter continues to have elastic hooks at the leg-hook interface with each hook intended to connect (impale) the vessel wall to resist migration. The hook is also intended to provide elastic deformation and straighten when the filter is pulled on for removal. The Meridian has caudal anchors laser welded at wrists of three of the arms, and at the shoulder of three arms. The caudal anchors are intended to help improve filter migration resistance in the caudal direction. The Meridian as with all the RNF is intended to be implanted in a patient with an IVC diameter of 28mm or less. The only change between the Eclipse and Meridian was the process added for laser welding of the titanium anchors to the arms. The Meridian and the Eclipse have the same jugular delivery system with the exception of the new spline cap added for the meridian with a larger in diameter and longer length to accommodate the added anchors to the Meridian filter.

622. Because the Meridian filter is produced with individual laser "welding caudal anchors" (3 on the arm wrist and 3 on the arm shoulder) onto an Eclipse filter, it was assumed by Bard that the radial force of the Meridian appendages (arms/legs) would be equivalent to the prior Eclipse/G2X. The

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<sup>747</sup> BPV-17-01-00149523 at 899

deflection parameters originally established based upon testing and FEA of the G2X, were utilized to evaluate both the G2X and Eclipse.<sup>748</sup>

623. TP-10-06-03 DV&V Test Report- MRI Evaluation of Meridian 8/5/2010. The purpose of the testing was to demonstrate that the Meridian IVC is “MR Conditional” when implanted in a patient exposed to a magnetic field strength of 1.5 Tesla and 3.0 Tesla as defined by ASTM F 2503-05. The other testing conducted by Bard was corrosion testing (TP-10-06-03) and galvanic corrosion testing of filter fragments to estimate the daily exposure of a patient to nickel from the Nitinol once implanted.
624. Corrosion testing is standard for the medical device industry making implanted metal devices. It reportedly has been done on Bard’s G2X and Eclipse filters to compare to Meridian. The titanium anchors would alter the surface area that was available for corrosion when compared to Eclipse. Corrosion testing is intended to provide information about the survival of a metal surface and biocompatibility when implanted permanently in the moist environment of a patient’s body. Corrosion testing also provides information in terms of the quality control procedures for manufacturing and cleaning a metal device before it is implanted. Six Meridian filters were selected for corrosion testing. All Meridian filter samples were twice sterilized by ethylene oxide (2X ETO) gas at Bard. As with Bard’s standard testing of its filter, there would be no simulation of the effects of transporting the commercial device before it is implanted. The Meridian testing was not conducted as a head-to-head comparison of Meridian to the G2X, Eclipse or the SNF. Instead Bard would compare Meridian to the historical data of G2X and Eclipse filters. Bard as standard for Bard also did not attempt to simulate environmental conditioning of an implanted environment for the Meridian to look at corrosion since the G2X had no environmental conditioning when it was tested. Therefore, the corrosion testing by Bard for its filters did not attempt to simulate the real-world implanted device. Corrosion testing was performed at an external laboratory DNV Columbus, Inc., Materials and Corrosion Technology Center, Dublin, OH.<sup>749</sup> Bard’s acceptance criteria for the filter surface stated:

*The corrosion pitting margin ( $E_b - E_r$ ) of the Meridian Filter must be equivalent or better than the G2X Filter corrosion pitting margin when tested per ASTM F2129-06.<sup>750</sup>*

625. According to a later discussion of the Galvanic Corrosion testing TP-10-6-06, the samples were representative of finished goods with the exception that the anchors were not placed in the normal position on the shoulders and wrists for the arms but at the ends of the arms in order to

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<sup>748</sup> BPV-17-01-00149523

<sup>749</sup> BPV-17-01-00149523

<sup>750</sup> ASTM F2129-06 Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices. This standard is intended to be used on a device in its final and finished form, as it would be implanted in a patient. It is assumed that reference methods have already been used for screening the material. It is intended to be used on metals that have a high resistance to corrosion. (www.ASTM.org); 372-375\_BPVE-01-00818477

accommodate the test set up. The test was intended to detect the interaction between the titanium anchor and the Nitinol wire. The prototypes for testing were anchors welded to Eclipse filters taken from production with the addition of titanium anchors welded with the BPV laser (StarWeld Laser). The final Meridian product was to be welded using the GFO laser (LAS016) as production equipment

626. There was a Design Validation & Verification (Project #8120) originated by Brian Boyle, TP-10-06-12 titled “Diaphragmatic Flat Plate Fatigue and Corrosion Examination of the Meridian Filter.” It was an accelerated *in vitro* fatigue behavior test under simulated physiological conditions. The study was intended to support a regulatory submission. Twelve manufactured and packaged and 2XETO sterilized meridian filters would be used for testing. Since the device is 2X sterilized, it is assumed that the exposure to the 130F (54.4<sup>0</sup>) sterilization constitutes the “worst case scenario” for the temperature/stress standpoint, so no other environmental stimulation was performed. Transit simulation was also not performed because it is assumed that shipping will not alter the structural integrity of the loaded filter. Fatigue testing and corrosion was for 4 million cycles to simulate 10 years of implantation in a coughing patient. The check for corrosion after fatigue testing was visual using 40X magnification.
627. Testing included use of a 25mm ID fatigue tube with a 25mm lining of simulab (.7mm WT) (i.e. a smooth sock lining). With the caudal anchors on the arms, the filter exhibited torque due to the longitudinal rigidity of the tube, since the tube was rigid and did not stretch as the patient’s vena cava would, this behavior of torque with anchors was deemed by Bard as set up related and not representative of what would be expected in vivo. The prior filters in this set up without caudal anchors compressed radially with no evidence of torque. A pressure chamber was used to simulate the vena cava and filter behavior in vivo, so that the Meridian could be observed at various pressures. The testing showed that the deflection patterns of both the Eclipse and Meridian in the set up were identical. The Meridian caudal arms engaged in the simulated vena cava (with pressure) and the arms deflect radially, without evidence of torque. Regarding a patient, Bard wrote that the “filter may be subjected to cyclic radial expansion/compression due to these contractions.” Diaphragmatic fatigue testing is designed to simulate the fatigue on the filter due to the expanding and contracting vessel.
628. Bard compared the Meridian to the historical data in a 1994 medical article for Boston Scientific’s Stainless Steel Greenfield Filter (SSGF)<sup>751</sup> which Bard called the “gold standard” for IVC filter performance. This 1994 data published for SSGF showed “acceptable fatigue resistance when tested simulating an IVC deflections from 2.5cm to 1.0cm (25mm to 10mm) for up to **10 million cycles** with 1 out of 10 filters fracturing (**10%**). The load chosen was to mimic maximal physiological changes that could occur in the human vena cava such as coughing. “
629. In 2010, Bard indicated it had used the same method for testing the Denali IVC Filter, however, Bard did not provide comparator information for Denali to Meridian or to SNF. Bard’s duration of the testing, unlike the SSGF was less than half the cycles, approximately 4 million cycles which Bard indicated was equivalent to 10 years of exposing the filter to diaphragmatic movements in a coughing patient. Chronic cough represented the worst case scenario for Bard

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<sup>751</sup> Bjarnason, *Investigative Radiology*, 1994

(coughing at a frequency of 43 coughs per hour, which equals 3.8 million coughs over a 10-year period, rounded to 4 million). So Bard's simulation fatigue testing was used to simulate 10 years implanted in a coughing patient (per TM1141700). The testing was conducted in a simulated 25mm IVC.

630. Weld strength was examined after fatigue testing according to Bard was based on FDA's 1999 Guidance. The FDA's Guidance 1999, pre-clinical testing should be able to demonstrate "sufficient fatigue resistance of the filter design." Sufficient fatigue resistance applies to the intended life cycle of a permanently implanted filter, (i.e., the patients' life expectancy). Based on the 510(k) clearance the Meridian fatigue resistance should be substantially equivalent to the SNF:

#### 4. Filter Fracture

*The filter's response to worst-case scenario respiratory and diaphragmatic movements in the vena cava under simulated respiratory cycles should demonstrate sufficient fatigue resistance of the filter design. In addition, there should be an examination of corrosion resistance and weld strength following cycling.*<sup>752</sup>

631. Not referenced by Bard, the 1999 Guidance placed the obligation of adequate testing to develop the Meridian on Bard, as well as the obligation to be familiar with the known history of its RNF family of filters when compared to the performance of the permanent SNF. See 21 CFR § 820.30; 21 CFR § 820.20; 21 CFR § 820.100; 21 CFR § 820.198; 21 CFR § 803; 21 USC § 331(a)(b); 21 USC § 351; 21 USC § 321(n); 21 USC § 352(a)(f)(1)(2),(t).

*The necessary array of tests for a particular filter will depend, in part, on the specific design. Therefore, this document may not reflect the complete battery of pre-clinical testing necessary to qualify all filters/designs...The degree to which a proposed device is similar to a currently marketed filter will indicate the level of testing necessary, i.e., whether the design characteristics can be assessed via in vitro bench testing, in vivo animal testing, clinical testing or some combination of all three.*<sup>753</sup>

632. There is nothing in the product information used for Bard's family of RNF permanent filters that indicates to the physician that Bard anticipated a filter lifecycle of "ten years" for a patient in terms of the adequacy of the fatigue testing it did for selling a permanent filter. That information about testing would need to be provided to a physician with a patient that may have a life expectancy greater than 10 years. The device could be implanted but there would now be identification for the physician and the patient and a need for monitoring and removal prior to 10 years.

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<sup>752</sup> BPV-17-01-00149523

<sup>753</sup> 1999 FDA Guidance

633. After cycling the filters in the apparatus for 4 million cycles, Bard then conducted a Visual Post Test inspection using 40X magnification to look for evidence of rust, corrosion, pitting. According to Bard's Acceptance criteria, there must be no visual evidence of pitting, rust or corrosion in any of the fatigue tested filters following fatigue simulation.

*Acceptance criteria for Meridian Filter – the filter must be corrosion resistant. No corrosion present on the filter following cyclic fatigue testing. No pitting, rusting and other signs of corrosion visible on filters under minimum 40x magnification.*

634. The weld strength testing is simply can the anchor hold a 5.0lb weight attached to an "anchor" (TM 1141700) and hanging freely. If the anchor breaks, it is recorded as a failure.<sup>754</sup>

635. Test report TR-10-06-12 "Valsalva-Diaphragmatic Flat Plate Fatigue and Corrosion Examination of the Meridian Filter" (ASTM E739-91)<sup>755</sup> actually indicated that based on the FDA, Bard only needed durability testing for 10 years of implant life. The population addressed by FDA in the 1999 Guidance is different from the population marketed by Bard to physicians or as cleared by FDA. Bard had the Recovery, G2X, Eclipse, and Meridian and later its next generation Denali filters all cleared by FDA as substantially equivalent to a "permanent filter." There is nothing that indicates to physicians "permanent" means only 10 years. Further, Bard was marketing the retrievable filters off-label as acceptable as both permanent and retrievable filters suitable for implantation prophylactically in younger patient populations with a greater life expectancy than addressed by the FDA's Guidance or cleared by the FDA. As NMT indicated during the design of the NMT Recovery filter, it was not adequately studied in young patient populations with longer life expectancy and was considered a temporary filter to be removed within 12 weeks.<sup>756</sup>

636. The ASTM E739-91 recommended the use of 12-24 samples, Bard chose to use 12 Meridian filters. All samples passed.<sup>757</sup>

637. Despite this significant difference in the patient population for 510(k) clearance, the FDA does not indicate in the 1999 Guidance that durability testing should only be through ten years of implantation life. 21 CFR § 820.30 addressed adequate design controls based on both design inputs and outputs. The testing based on the anticipated lifecycle of an IVC Filter that is labeled and cleared as a permanent implant should have testing through the anticipated implant lifecycle to ensure adequate design and performance, namely an anticipated patient lifetime. Instead, Bard has used FDA has asserted it can cut off testing after only a ten-year life cycle.

638. Again, the testing of the Meridian should have been compared to Bard's SNF, a permanent implant predicate to ensure substantially equivalent performance. Bard wrote its unsupported statement about 10-year testing:

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<sup>754</sup>BPV-17-01-00149523

<sup>755</sup> ASTM E739-91 Standard Practice for Statistical Analysis of Linear or Linearized Stress-Life (S-N) and Strain-Life (e-N) Fatigue Data.

<sup>756</sup> BPVE-01-00066044

<sup>757</sup> BPV-17-01-00149523

*Per the FDA Guidance Document-Cardiovascular Intravascular Filter 510(k) Submissions, the filter durability must be proven safe in vivo for up to ten (10) years of implantation life. Accelerated in vitro-fatigue testing is conducted in order to demonstrate this is a reasonable amount of time.*

*Previous testing of the Eclipse filter utilizing the same deflection parameters and demonstrated that the Eclipse filter was safe up to ten (10) years of implantation.<sup>758</sup>*

639. For this testing, all samples were visually examined (40X) for fracture, corrosion. The 5lb weight was used for the shoulder of the anchor, the wrist of the anchor, the leg and arm. The tensile strength of the anchor weld at the shoulder or wrist of the filter arm was to be  $\geq 5$ lbs.

640. Bard wrote that for the device:

*The highest stress point on the filter occurs at the neck area where the arms exit the snare tip. During flat plate loading, two (2) of the filter arms (arms perpendicular to deflection) experienced the highest strain points. Based on the twelve (12) filters tested, this equated to 24 high stress points.<sup>759</sup>*

641. This test was conducted at 15Hz for the 4million cycles in a tube of 25.02mm diameter to simulate 10-years implantation in a patient using 12 filters. Post fatigue testing, all the shoulder anchors supported the 5lb weight (36/36). However, one of the wrist anchors (1/36) (3%) separated away from the wire after the 5lb weight with the arm wire fracturing at the weld (failure). The wire was inspected at the weld and found to be within specification. The inner diameter of the anchor was found to be within specification. Visually, the weld had minimal weld penetration on the wire surface (was out of specification). This was not an area identified by Bard as a high stress point for the filter.<sup>760</sup>

642. Based on destructive testing and visual examination, Bard blamed the weld failure on a poor weld. The most probable cause was an off-center welding technique used manufacturing the samples. At the time of the production of the test filters, the welding technique still had not been validated. The recommendation was that the laser welding process be validated and process controls be explored.

643. The conclusion was that based on the data, the Valsalva-diaphragmatic in vitro-fatigue testing results demonstrate the long-term in-vivo safety of the filter at a duration of up to ten (10) years.<sup>761</sup>

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<sup>758</sup> BPV-17-01-00149523

<sup>759</sup> BPV-17-01-00149523

<sup>760</sup> BPV-17-01-00149523

<sup>761</sup> BPV-17-01-00149523

644. In terms of the Bard's Quality Control of bioburden, monitoring of product bioburden was only to begin with the Meridian Filter. Document No: CQA-STD-13 Revision No:01 Corporate Quality Manual, 2011:

*The validated product (Eclipse Filter) is not currently in the Global bioburden program and is not being tested by Bard Shared Services; therefore, there are no established alert and action limits for the device. However, moving forward, the validated and/or candidate product will be included in the Global bioburden program with the standard 300 CFUs/SIP alert limit and 1000CFUs/SIP action limit until there is enough data to calculate appropriate limits for this device. The candidate product has a greater bioburden than the current alert limits for the validated device; therefore, this device will become the master product code representative of the worst-case device for the overall product family upon its incorporation into the Global program.<sup>762</sup>*

645. Biocompatibility Requirements (BR-8120) of the Meridian was based on the same Biocompatibility requirements for the Eclipse other than for the addition of the titanium anchors supplied by Tegra (TP-10-04-29), overseen by Micky Graves.

646. Biocompatibility testing for the anchors was chemical extraction testing TD-01421 to ensure the Eclipse Anchors Filter did not elute any chemicals that appear on the California Proposition 65 list and to demonstrate that the filter was exhaustively extracted within 24 hours at 37<sup>0</sup> C. The testing was completed on 1 device based on ISO-10993-1 obtained from GFO. The device was considered to have passed ISO-10993-1.

647. The Meridian Design History File, Project #8120 TD-01964 July 18, 2011, from Brian Boyle has a "Bench Top Tilt Testing of Competitive Filters." Testing was conducted on the Meridian, Eclipse, Celect, Tulip, and Option Filters. The Celect and Tulip were used for competitive benchmarking since the Cook filters represented the significant competition to Bard for the "optional filter" market. It is interesting to note that the Eclipse/Meridian (48.0) have the shortest filter heights of the optional implants examined.

648. TP 10-08-09 was DV&V Caudal Migration Testing of Meridian and Optease (Cordis) Filters. The Optease is a retrievable filter up to 14 days post implantation. Clinical trials with the Optease have indicated that the filter is resistant to caudal migration.

#### **E. Denali: Bard's latest generation filter.**

649. Bret Baird worked at Bard from 2006 through 2011. He began as a project manager, then franchise manager and in 2008 Marketing Manager for IVC Filters. He left Bard in 2011. He was the author of Bard's Idea POA for Project #8101, Project Name Denali Filter, dated August 2009.<sup>763</sup> The project goal was to create a filter with improved performance to Bard's G2X. He wrote: "Offering a device with improved resistance to movement, fracture and penetration, while

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<sup>762</sup> BPV-17-01-00149523, at 761, also 766

<sup>763</sup> Baird Exhibit 320

managing long-term retrievability will help strengthen our position and capture more share.” The most common inputs from customers (physicians) to the Sales Force was for the G2 and G2X to improve retrievability, filter migration, tilt, and penetration. To help reduce fracture and reduce complications, the project would incorporate design changes thought to help limit movement, keep the filter centered, and minimize fracturing. The modifications proposed in 2009 for the Denali filter included:

- Penetration limiters
- Caudal anchors
- Laser-cut one piece design
- Electropolished finish
- Enhanced design with broad shoulders for centering.<sup>764</sup>

650. Mr. Baird said the “Situation” was that physicians were very sensitive to complications with optional IVC filters which makes it difficult to retrieve or increase the risk for patients. Physicians decide to place filters in patients and what filter technology to use based on a risk/benefit tradeoff. He then wrote for “Problem” that the *“Bard G2 and G2X filters have a reported rate of 12% caudal migration in the EVEREST trial, though the reported incidence rate of G2 filter fractures is low, the severity of fractures can be significant, a fractured arm or leg has the potential to travel from vena cava to the heart or lungs.”* The “Need” for marketing according to Mr. Baird was a *“filter that delivers the same performance characteristics as the current design but with a higher resistance to fracture and movement.”*<sup>765</sup>

651. His project plan was to position the Denali as a new platform, breaking from offering the current product. The message for the customer was that Bard had built on the past product to offer a new product with the same benefits: caval centering, dual filtration, long-term reliability, and multiple retrieval options with the same enhanced performance. He continued, *“To get to market faster we will first position it as a new reliable and easy to use permanent filter and follow a year later with a claim of long-term retrievability and multiple retrieval options. The Denali was to come to the market as a permanent filter and sold along with Vail (Eclipse) until a retrievable option is obtained. At that point the Vail will be completely phased out and sales replaced by Denali.”*

**XI. BASES FOR OPINION #5: BARD’S QUALITY SYSTEMS (QS) AND POST MARKET MONITORING PROCEDURES WERE FLAWED, HELPED UNDERESTIMATE RISK, AND PERMITTED CONTINUED COMMERCIAL RELEASE OF MISBRANDED AND DANGEROUS PRODUCTS AS SUPPORTED BY BARD’S RECEIPT OF AN FDA 2015 WARNING LETTER.**

FDA issued a July 13, 2015, Warning Letter to Bard following inspections in 2014 of its Glens Falls, New York and Tempe, Arizona facilities. FDA observed serious problems in Bard’s manufacturing and quality management systems. Problems identified included Adulteration/Misbranding violations, Quality Systems Regulation violations, and Medical Device Reporting violations. The

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<sup>764</sup> Baird Exhibit 320

<sup>765</sup> Baird Exhibit 320

observations identified by the FDA's inspector are consistent with Bard's employee testimonies and Bard's internal regulatory documents.

***Applicable Regulations:*** 21 CFR § 820.198; 21 USC § 352(t)(2); 21 USC § 360i, 21 CFR Part 803; 21 CFR § 820.50(a) 21 CFR § 820.75(a); 21 CFR § 820.80(b); 21 CFR §§ 803.50(a)(2), (b)(2)(3); 21 USC § 331(a)(b)

652. Chad Modra, Director of Quality Assurance (QA) for BPV since 2012 described his position as including corrective and preventive action systems and post-market quality assurance.<sup>766</sup> He was produced by Bard as the individual most knowledgeable about the FDA's 2015 Warning Letter to Bard and Bard's response. His immediate supervisor is Gin Schulz, VP of Quality for Bard's Corporate Office, who formerly occupied Mr. Modra's position at BPV. Before moving to Arizona, he had been at Bard St. Lake City as Director of Quality Engineering. He testified that Bard has internal procedures and instructions regarding risk management standards for field assurance, complaint handling, and post-market surveillance, which is part of the complaint and investigation and Medical Device Reporting (MDR) procedures.<sup>767</sup> He has never personally investigated and completed a complaint file of a potential adverse event relating to an IVC filter and he is uncertain whether Ms. Uebelecker ever did this either.<sup>768</sup> He is uncertain if Ms. Judy Ludwig has ever personally investigated a complaint because her job is focused on the logistics and oversight of the process as a whole.<sup>769</sup> He knows Mr. Wheeler has personally investigated and completed a complaint file of a potential adverse event relating to an IVC filter.<sup>770</sup> A team of biomedical and biomechanical/mechanical engineers work on investigating and analyzing root cause of potential complaints/malfunctions of IVC devices, while degreed engineers carry out the complaint investigations.<sup>771</sup> Mr. Modra testified that Shand Gad is the toxicologist consulted by Bard and Scott Trerotola the clinician.<sup>772</sup>

653. Complaint handling and field assurance are the same at Bard. Part of QS involves the maintaining of complaint files, use of statistical trending and identification of Corrective and Preventive Actions to result issues with a product and return the product back to compliance with the Act. Corrective and preventive actions can include a spectrum of actions including failure investigations, investigation of design, manufacturing changes, Dear Doctor letters, recalls, and updating the label and marketing. Complaint files are required to be maintained as part of day to day business. There is to be a process to review complaints and file required Medical Device Reports to the FDA. 21 CFR § 803.

654. Judy Ludwig testified regarding the adequacy of Bard's postmarket surveillance practices. Ms. Ludwig has been the Senior Manager of Field Assurance for two years as a member of Bard's Field Assurance, with 31 people working in her department and seven directly report to her. She

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<sup>766</sup> Modra deposition Vol I, p.23, L.7-9

<sup>767</sup> Modra deposition Vol I, p. 36, L. 11-20

<sup>768</sup> Modra deposition Vol I, p.45, L6-10

<sup>769</sup> Modra deposition Vol I, p.44, L10-22

<sup>770</sup> Modra deposition Vol I, p.44-45, L24-5

<sup>771</sup> Modra deposition Vol I, p.45, L11-25

<sup>772</sup> Modra deposition Vol I, p.67-68, L 22-3

started with Bard in 2012, and directly reports to Maureen Uebelacker. Before joining Bard she worked at Fed Ex. She has no formal education, training, or experience in medicine and no experience with the FDA. Bard's tracking and trending information is considered propriety information and Bard does not make it available to physicians. Ms. Ludwig agreed that her complaint investigation role requires looking at whether those thresholds have been exceeded. Exceeding a threshold is "potentially" a red flag that there is a problem with the product. She agrees that a red flag can potentially show product problems that may impact safety.<sup>773</sup> To look for a threshold for expected migration of IVC devices, Ms. Ludwig would look at Bard's Design Failure Modes and Analysis [DFMEA] document.<sup>774</sup> Bard has created DFMEAS for RNF, G2, G2Express, SNF, Meridian, and Eclipse. Bard's Clinical Severity Matrix is important for informing senior management about the severity and frequency of various injuries.<sup>775</sup> In 2014 Bard added a clinical specialist in 2014 because there was an increase in filter complaints. Dana Stegmeier, Nurse, works at Bard. There are 2 other RNS as well-Laura and Zenya.<sup>776</sup> There is no doctor in the department. They do have a Medical Director, Dr. Altonaga<sup>777</sup> but no access to a radiologist.<sup>778</sup> She relies of the DFMEA for the acceptable threshold for frequency of an event like limb fracture.<sup>779</sup>

655. The Field Assurance specialists take customer calls and initial complaint information. They evaluate/review what gets reported to the department and log these events into the complaint management system, TrackWise. These specialists collect data for all the products that Bard/BPV manufactures. Bryan Vogel, Senior Clinical Field Assurance Specialist and John Wheeler, Field Assurance Engineering Manager as the 2 supervisors. John Wheeler replaced Natalie Wong, who had headed the Engineering Group as Field Assurance Engineering Manager, and he was hired December 2012.

656. Through product training prior to device launches is how Ms. Ludwig learned about risks and benefits, including that patients can potentially suffer fracture with migration of fractured parts, but she could not recall what would stop fractured fragments traveling in patients.<sup>780</sup>

657. Ms. Ludwig was not specifically taught during product training that the ability of devices to perforate vascular structures is potentially a serious complication, nor did she learn about it on her own. Bard gave Ms. Ludwig no training whatsoever on the ways in which a filter malfunctions can cause bleeding, hemorrhaging or death or the ways in which a malfunction will require surgery. Ms. Ludwig doesn't think knowing that information is necessary for her job.<sup>781</sup>

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<sup>773</sup> Ludwig deposition 7/27/16, p. 33, L. 2-20

<sup>774</sup> Ludwig deposition 7/27/16, p. 34-36, L. 25-1

<sup>775</sup> Ludwig deposition 7/27/16 p. 76-79, L. 25-4

<sup>776</sup> Ludwig deposition 7/27/16 p.83-84, L. 21-23

<sup>777</sup> Ludwig deposition 7/27/16, p. 138-139, L. 20-14

<sup>778</sup> Ludwig deposition 7/27/16, p. 145, L. 7-22

<sup>779</sup> Ludwig deposition 7/27/16, p. 180, L. 5-22

<sup>780</sup> Ludwig deposition 7/27/16 p. 37-38, L. 4-16

<sup>781</sup> Ludwig deposition 7/27/16, p. 38-40, L. 18-5

658. Ms. Ludwig said that Bard has a “Clinical Group” that she believes is aware of clinical risk information about the filters. Injury severity for a device is not tracked and trended. She testified that Bard only tracks malfunctions, not injury. They do not track patient outcome for injury in patients.<sup>782</sup> She also said that the Engineering Group gathers complaint data. Reports are generated out of the Engineering Group within Field Assurance, John Wheeler is the head, and these specialized reports can pull out of information on injury frequency. Bryan Vogel, not a radiologist, looks at the X-ray films to determine if the films show filter limb perforation.<sup>783</sup>
659. A primary goal is to revolve around timely reporting, the “reportability decision tree”<sup>784</sup> which mandates the time from which a complaint is entered that a decision should be made on whether it’s a reportable event that requires the submitting of a MDR to the FDA. There is no target numbers with regards to how many complaints a specialist or the group should handle.<sup>785</sup>
660. Regular reports generated from Ms. Ludwig’s department that she reviews include a red/green light report which identifies the type and number of complaints for all product families and any issues or “anomalies.” The report goes to corporate. An anomaly would be four reports coming from the same hospital or frequency of particular injury. She doesn’t approve the report. She reviews it for “awareness” on monthly basis. She reviews a list of MedWatch or 3500A forms that were submitted to FDA, on monthly basis.<sup>786</sup>
661. Bard’s procedure for addressing the situation when a Complaint Information or Complaint Summary says that a definitive root cause is unknown. In Ludwig’s personal experience, she has never seen an IVC complaint determine that filter design defect is the root cause of injury, nor she does not remember ever hearing that from anyone at Bard. She has never recalled seeing manufacturing defect cited as a root cause. She can’t recall a time she reviewed an IVC filter report where a root cause was anything other than unknown.<sup>787</sup> This is not a statement that would be consistent with Bard’s responsibility to conduct an adequate investigation for a reported event, even if classified a ‘malfunction’ and develop an effective CAPA.
662. Ms. Ludwig was asked about who makes the decision whether a device is performing as safely as intended. She testified that Bard uses the established acceptance thresholds listed in their design and risk documentation. Field Assurance makes the assessment on whether devices perform consistent with those established thresholds. This is part of the Bard investigation process. One element is to review the DFMEA for a particular failure mode and to calculate a rate to see if it’s below or above the threshold.<sup>788</sup>

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<sup>782</sup> Ludwig deposition 7/27/16, p. 40-43, L. 6-18

<sup>783</sup> Ludwig deposition 7/27/16, p. 170-172, L. 16-25

<sup>784</sup> Ludwig deposition 7/27/16, p. 99, L. 25

<sup>785</sup> Ludwig deposition 7/27/16, p. 99-100, L. 2-6

<sup>786</sup> Ludwig deposition 7/27/16, p. 100-104, L. 13-6

<sup>787</sup> Ludwig deposition 7/27/16, p. 170-175, L. 16-7

<sup>788</sup> Ludwig deposition 7/27/16, p. 258-259, L. 25-14

**A. FDA ISSUED A JULY 13, 2015 WARNING LETTER CITING BARD'S  
FAILURE TO SUBMIT MDRS AND INVESTGATE COMPLAINTS**

663. From November 18, 2014, through January 15, 2015, the FDA inspected the BPV facility in Tempe Arizona. And it also inspected Queensbury, NY facility on October 6, 2014, through November 25, 2014. According to Mr. Modra, the BPV names on FDA's "483"<sup>789</sup> are Judy Ludwig and John Wheeler.<sup>790</sup> Ms. Uebelacker is in charge of the managers for the investigations of complaints and complaint handling, and Mr. Wheeler and Ms. Ludwig report directly to her. According to Mr. Modra, neither Uebelacker, Wheeler, Ludwig or himself have any medical training.<sup>791</sup> The FDA's inspection was unannounced and Ms. Perkins requested a list of complaints on CD and other documents. She stayed a few days and then went offsite to review the information she requested.<sup>792</sup>
664. On July 13, 2015, FDA's Los Angeles District sent a Warning Letter to Timothy Ring, Chairman and CEO of Bard. Ms. Perkins after her 2014 inspection issued a 483 with objectionable findings. The Warning Letter was sent when Bard's response to the 483's findings were not found to be acceptable. The products inspected were the SNF and the Denali IVC Filter and Recovery Cone Removal kit. The Warning Letter addressed violations found at both the Tempe facility and the Queensbury facility. According to Ms. Ludwig, Ms. Perkins looked at less than 50 reports.<sup>793</sup>
665. FDA cited that the devices are adulterated in that the methods, facilities or controls used to produce the devices are not in conformity with current good manufacturing practice requirements of the Quality System. Among the QS violations included Bard's failure to establish and maintain procedures for receiving, reviewing and evaluating complaints. 21 CFR § 820.198. The FDA's discussion included that a death reports and serious injuries were filed as a malfunction and not an injury. Complaints do not include adequate information about the events. FDA found responses to FDA's findings by Bard were not acceptable or adequate. Another heading for the Tempe AZ facility was "MDR Violations" with devices are misbranded in that the firm failed or refused to furnish material or information regarding the devices that is required and MDR. FDA cited the BPV facility for failure to submit MDRs. MDRs filed are submitted with incomplete or missing information.<sup>794</sup>
666. Mr. Modra determined that to respond to FDA Bard would look at two years of complaint records from 1/1/13-1/8/15. Mr. Modra did not review the 939 complaints files himself.<sup>795</sup> Bard communicated this action to FDA.<sup>796</sup> For 939 reports reviewed, a total of 274 additional serious

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<sup>789</sup> FDA Form 483 is a form the FDA uses during inspections.

<sup>790</sup> Modra deposition Vol I, p.39, L12-17

<sup>791</sup> Modra deposition Vol I, p.42-43, L25-4

<sup>792</sup> Modra deposition Vol I, p.81-87, L5-25

<sup>793</sup> Ludwig deposition 7/27/16, p. 220-221, L. 13-10

<sup>794</sup> Exhibit 322

<sup>795</sup> Modra deposition Vol I, p.184, L5-7

<sup>796</sup> Ludwig deposition 7/27/16, p. 204-207, L. 3-18

injury files reported after the review. 230 converted to serious injury. It is unclear whether the other 44 are changed to malfunction reports. This was a 24.5% spike in serious injury reports.<sup>797</sup>

667. According to Mr. Modra, Ms. Ludwig, and Mr. Wheeler, under his direction worked on changing two things: their procedures and how training was conducted, which is why their names appear on the 483 notice at BPV. The BPV team at Bard provided Modra with the information needed to write out the responses to the warnings and 483 letters to the FDA. He only really collaborated with King and Spalding and Hogan Lovells to insure that all the FDA's questions were being met.<sup>798</sup> Mr. Modra never wrote a letter to the FDA saying that Bard disagreed with the FDA's assessment of its system.<sup>799</sup>

668. Modra employed outside counsel from Hogan Lovells and King & Spalding before the 483s were received to help write responses to both the 483s and the Warning Letter because both firms employ former FDA employees who are experts in conveying the FDA's expectations.<sup>800</sup> In 2011 Modra reached out to Steve Niedelmann, who used to work for the FDA, at King & Spalding, and due to his former experience, Modra believe he was a good resource to contact from time to time about helping him carry out his day to day responsibilities as a quality assurance professional according to FDA regulations. Modra has continued to use Niedelmann as a resource on "speed dial."<sup>801</sup> Neither King and Spalding or Hogan Lovells have performed a site visit. The Bard site visit overview provided to them did not include the 42 files chosen at random and reviewed by FDA.<sup>802</sup>

669. The only other people he has reached out to for responding to FDA was a toxicologist for the extraction testing and a clinician to weigh in on the clinical nature of some of the events cited in the original 483 for BPV.<sup>803</sup>

## **B. BARD HAS A DUTY TO MONITOR THE MEDICAL LITERATURE REGARDING RISKS FOR ITS DEVICES, REPORTING AND UPDATING SAFETY INFORMATION**

670. Ms. Raji-Kubba was asked about the role of Bard for patients already implanted with Bard's device. She stated that Bard's responsibilities including investigating every complaint received, reading available literature, and consulting with clinicians to try to get more information. She was shown the Kalva (2006)<sup>804</sup> article about RNF published by a group of scientists and physicians at Massachusetts General Hospital in Boston. She testified, "I haven't read it." It was a case series of 96 patients that had been implanted with Bard RNF. She was unaware of any

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<sup>797</sup> Ludwig deposition 7/27/16, p. 209-219, L. 9-8

<sup>798</sup> Modra deposition Vol I, p.55-56, L16-2

<sup>799</sup> Modra deposition Vol I, p.95, L16-23

<sup>800</sup> Modra deposition Vol I, p.46-48, L. 15-3

<sup>801</sup> Modra deposition Vol I, p.48-50, L21-13

<sup>802</sup> Modra deposition Vol I, p.66-67, L17-2

<sup>803</sup> Modra deposition Vol I, p.65, L14-20

<sup>804</sup> Kalva SP, Athanasoulis CA, et al. "Recovery" vena cava filter: Experience in 96 patients. *Cardiovasc Interven Radio* 2006 Jul-Aug; 29(4):559-64; Kubba Exhibit 299

times where Bard asked any hospitals to do a study like this. The conclusion was that “filter arms penetrated the IVC wall in 11, which is 27.5% of patients.” She was asked if this should have been part of the medical literature that Bard was reviewing. She says that each one of the patients with an issue was likely logged as a complaint that was reviewed by Bard. Ms. Raji-Kubba confirmed that during her time at Bard as VP of R&D (2007-2011) she was not aware of Bard taking the initiative to request every hospital that had patients with Bard filters to evaluate the integrity of the filters and status of the filters.<sup>805</sup> 100% of the patients in this case series had perforations.

671. Ms. Raji-Kubba was shown Hull (2009),<sup>806</sup> also a published paper dealing with the RNF. She recalled the publication; “it got attention, to make sure we’ve logged in all these complaints.” This was an example of a single hospital case series of patients that had received the RNF. A significant % of patients were shown to have perforations, diagnosed by CT scan. She affirmed that Bard never asked hospitals to perform CT scans on patients to determine if there were perforations, migrations or fractures. A patient presented to the hospital with symptomatic filter arm fracture and migration and eventually had the remaining filter removed. Following that, a second patient came to the hospital with the same problem. That triggered the hospital to begin contacting and following up on all patients implanted with Bard RNF. She said if the physicians had reported the problem to Bard, it would have been entered as a complaint. The fracture rate in the study ultimately was 21%.<sup>807</sup> Ms. Raji-Kubba had a role for tracking complaints and “can assure you the complaint rate was not 21%.”<sup>808</sup> The conclusion of the authors was that Bard RNF was associated with increasing rates of limb perforation, arm fracture, and migration, in their small study population. They recommended CT scans for monitoring all patients implanted with RNF. According to Ms. Raji-Kubba, Bard has not discussed the use of CT scans by physicians for monitoring filter status in implanted RNF patients.<sup>809</sup>

672. When asked “in the patient, if there’s a fracture, is that a good thing or a bad thing?” she responded that Bard designs products so they don’t fracture under use conditions.

673. Ms. Raji-Kubba was also asked about Nicholson (2010),<sup>810</sup> another published article about RNF with co-authors from York Hospital including Dr. Agarwal. Ms. Raji-Kubba had visited with Dr. Agarwal at York Hospital. The publication was about cardiac perforation as witnessed symptoms. Ms. Raji-Kubba confirmed that Bard did not ask Dr. Agarwal to conduct the study. There is a May 2009 email from Bill Edwards to Ms. Raji-Kubba and Mike Randall discussing an upcoming meeting with Dr. Lynch. Dr. Lynch was interested in discussing the addition of ‘electropolishing’

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<sup>805</sup> Raji-Kubba deposition 7/18/16, p. 38-52, L.10-6

<sup>806</sup> Hull JE, Robertson SW Bard Recovery filter: Evaluation and management of vena cava limb perforation, fracture, and migration. *J Vasc Interv Radiol* 2009 Jan; 20(1):52-60; Kubba Exhibit 300

<sup>807</sup> Raji-Kubba deposition 7/18/16, p. 52 -63, L.7-5

<sup>808</sup> Raji-Kubba deposition 7/18/16, p. 65-75, L.4-6

<sup>809</sup> Raji-Kubba deposition 7/18/16, p. 72-75, L.19-6

<sup>810</sup> Nicholson W et al., Prevalence of Fracture and Fragment Embolization of Bard Retrievable Vena Cava Filters and Clinical Implications Including Cardiac Perforation and Tamponade, *Arch Intern Med.*, Nov. 8, 2010, 170(20), at 1827-31; Kubba Exhibit 302

the filters. The email continued “*after we meet with Dr. Lynch, we’re going to go to York, PA and meet with Dr. Agarwal. Dr. Agarwal has lots of experience placing both Simon Nitinol and G2 filters.*” Dr. Agarwal at that time was concerned about fractures and migrations. Ms. Raji-Kubba confirmed she met with Dr. Agarwal at his office.

The Hull, Kalva, and Nicholson publications are all physician case series which followed-up on patients implanted in RNF. Such observational information can be obtained by Bard opening a registry, or using a large insurance database to obtain post-market safety information. FDA was requesting the same type of information when it issued its 522 Order and Bard chose to enter the PRESERVE study. There was nothing that would have prevented Bard in 2002 from taking steps to voluntarily obtain such required post-market performance information following launch of the RNF to update its label and marketing and ensure patient safety.

**XII. BASES FOR OPINION #6: BARD ENGAGED IN AGGRESSIVE OFF-LABEL PROMOTIONS WHICH OVERSTATED BENEFITS, DOWNPLAYED RISKS, EXPANDED THE IMPLANTED PATIENT POPULATION, AND FAILED TO ADEQUATELY WARN PHYSICIANS, PATIENTS, AND ITS OWN SALES FORCE OF THE RISKS.**

Bard engaged in improper and illegal promotion and marketing of its RNF filters for off-label uses which changed the intended patient population, expanded the number of new and healthier patients unnecessarily implanted with defective Bard IVC Filters. Such actions began prior to Bard’s 510(k) clearance of the RNF and continued throughout Bard’s aggressive promotion of the RNF family of IVC Filters all without providing adequate risk information to physicians or patients.

***Applicable Regulations:*** 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n); 21 CFR § 801.109; 21 USC § 351(f)(1)(B); 21 USC § 360(e); 21 USC § 360(k); 21 CFR § 807.81(a)(3)(ii); 21 CFR § 801.4

674. Since 1976 and the passage of the Medical Device Amendments to the Federal Food and Drug Act, Congress assigned the FDA the role of pre-market gatekeeper to oversee the entry of new medical devices to the United States. The FDA has also been made the pre-market gatekeeper for the indications and intended use a medical device can be marketed for to the public in adequate support for safety and efficacy. The 510(k) clearance letter provided the legal indications for use to the manufacturer for marketing in the United States. The FDA also is to clear new marketing claims for products based on the sponsor having provided substantial scientific evidence.

675. Prescription devices are required to provide an adequate prescription label to the health care provider. 21 CFR § 801.109. The manufacturer is responsible for ensuring the adequacy of its own label and marketing. In terms of a manufacturer selling a misbranded or adulterated medical device, that is considered a Prohibited Act. 21 USC § 331(a)(b). Devices are adulterated, 21 USC § 351, when they do not perform as cleared for marketing by the 510(k) (or approved by a PMA) or when sold without obtaining the necessary pre-market clearance or approval or for significant risk devices used for investigational new indication first require approval of an Investigational Device Exemption (IDE) and its safeguards. 21 CFR § 812. Devices are also adulterated when they have been manufactured under conditions that do not adhere to accepted

Good Manufacturing Practices of the Quality System Regulations (GMP/QS), 21 CFR § 820, and the company's own standard operating procedures (SOP).

676. Devices are misbranded when promoted or advertised for a new unapproved indication or with overstatement of claims not approved or cleared, with false and misleading information and inadequate warnings and precautions. Misbranding can also take into account anything written, oral or implied about a product. That would include statement and actions of a company, its sales force or individuals representing the company. Misbranding can include false and misleading statement published in the medical literature missing important safety and performance information, or failure of a company to disclose its involvement in writing an article or training materials which fail to provide adequate and balanced information. Devices are also misbranded when the manufacturer has not provided required, adequate and truthful reports to the FDA. 21 USC § 321(n); 21 USC § 352(a)(f)(1)(2)(t).

677. For IVC Filters, in its 1999 Guidance the FDA required all IVC filter manufacturers selling permanent IVC filters after 1999 to update its labeling and marketing to reflect only the following four cleared indications for use. These four indications remain the same cleared indications for marketing of IVC Filters permitted the IVC filter industry in 2017:

- Pulmonary thromboembolism when anticoagulants are contraindicated
- Failure of anticoagulant therapy in thromboembolic diseases
- Emergency treatment following massive pulmonary embolism where anticipated benefits of conventional therapy are reduced
- Chronic, recurrent pulmonary embolism where anticoagulant therapy has failed or is contraindicated.<sup>811</sup>

678. These are the same cleared indications permitted for Bard's legal marketing of its IVC Filters. All other marketing and claims are considered "off-label" and not permitted by the Act to be made by the manufacturer. However, Bard's off-label marketing for new prophylactic indications in different patient populations essentially change the intended use of IVC Filters without clearance or approval by FDA. Manufacturers upon becoming aware of a change in intended use are required to update its own labeling and ensure the safety of the public and the adequacy of its label. 21 CFR § 801.4. Bard failed to do this and engage in aggressive off-label promotion despite the risk for the public.

679. When RNF was cleared as a permanent filter, Bard agreed to the following statement that was to occur in its labeling and marketing for RNF:

*The safety and effectiveness of the device for use as a retrievable or temporary filter had not been established.*<sup>812</sup>

680. Bard was on notice that beginning at its clearance of December 20, 2002, it was not to promote the RNF for off-label retrieval or temporary use.

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<sup>811</sup> 1999 Guidance

<sup>812</sup> BPV-TRIAL-EXHIBIT-1245\_00001-00003

**A. Bard has a duty to be truthful and not promote for off-label uses.**

681. Mr. DeJohn was a VP at Bard from 2000-2008. He agreed that the primary concern of a medical device company should be safety and should come before profits. He agrees the company is in a position to have knowledge and know-how about the products, although claims ultimately the clinicians are in the best position to understand the risks based on background/education. The Company is obligated to provide fair and accurate information about the product. Important to be truthful, relay critical factors, instructions for use, and educate. He stated that the sales reps are the face of the company, the main contact for clinicians, and must be truthful. FDA dictates the framework of what the sales rep can say. FDA must approve a product. The company cannot promote or sell the product for a use not approved by the FDA-off-label. Doctors on their own can use the device off-label. If a sales rep promoted off label use, then he would be disciplined. The company made sure the sales reps followed federal regulations. Sales reps followed information delivered from the company. Says the sales reps would get information on device from multiple sources- project managers, industry journals, etc.<sup>813</sup>

682. Bard would control how to position its products for physicians. Bard more or less dictated the features and benefits as well as the risks. The sales reps relied on people above them to get accurate information and relay that to doctors. Most information that sales reps were expected to provide would come from Bard itself- how to sue the device, what patients the product is indicated for, all of which is in the IFU. They were expected *“to be able to engage a clinician in a conversation about...what their decision-making algorithm looks like right now, what device they currently use, what types of patients do they use filters on, what areas are they concerned about, and ultimately get to place where we want to derive value that we can provide the clinician.”*<sup>814</sup>

683. Mr. DeJohn continued that Bard would sometimes give FAQs to sales reps. Some FAQs were for sharing with physicians (especially if there was a fairly sensitive topic), because doctors relied upon that information to treat their patients. The latter information would also be shared through training sessions with sales reps. There were national sales meetings where product would be discussed and monthly conference calls. Bard gave sales reps laptops and maybe cell phones and emails was one source of information for sales reps. Bard had programs that allowed them to see their performance and objectives. Bard also shared anything it wanted with them in writing via email. Sales reps were not required to keep track of how many times they met with Dr. XYZ or Dr. XYZ's staff, but some may have. Depending on the question a doctor would ask, Bard sometimes gave sales reps information they were specifically supposed to relay.<sup>815</sup>

**1. Bard's interactions with Dr. Asch as Bard's KOL.**

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<sup>813</sup> DeJohn deposition 6/17/16 p. 12-22, L. 7-1

<sup>814</sup> DeJohn deposition 6/17/16 p. 27-31, L. 2-25

<sup>815</sup> DeJohn deposition 6/17/16 p. 32-41, L. 1-3

684. Dr. Murray Asch was a key opinion leader (KOL) for Bard. Mr. DeJohn recalls that Dr. Asch “did the early work” studying the RNF. He recalled that there was a fracture with a pregnant patient in the first Dr. Asch study. He did not recall the migration of the second fracture. DeJohn did not know, and does not believe, that Asch told Bard he had safety concerns regarding the RNF. He thinks if Dr. Asch had told Bard that, he believes Bard would have responded appropriately. He can image that Dr. Asch would have shared priorities for a next-generation device, but it hard to image that Dr. Asch told Bard that it should improve the Recovery before putting it on the market. He does not know whether Bard told Dr. Asch that it would do a large multi-site clinical trial before taking the RNF to market. He does know that Bard did no such trial, although what Bard did was what was required by the FDA to get clearance/commercialization.

685. Mr. DeJohn continued about Dr. Asch, that he does not know that Bard never told Dr. Asch about the Recovery-Related injuries and deaths that it learned of. He does not know that Dr. Asch became angry and quit using Bard filters.<sup>816</sup>

## **2. Complaints of Bard’s sales reps misinforming doctors.**

686. Mr. DeJohn was asked if Bard “lied” to doctors what would occur. His response was that if Bard “lied” to doctors, the doctors would get upset with Bard and feel wronged. He was often brought into any situation where there were upset doctors. He was sometimes told by sales reps when doctors “were no longer going to use a Bard product.” He was sometimes told specifically that doctors were “extremely angry” about the Recovery or G2.

[REDACTED]

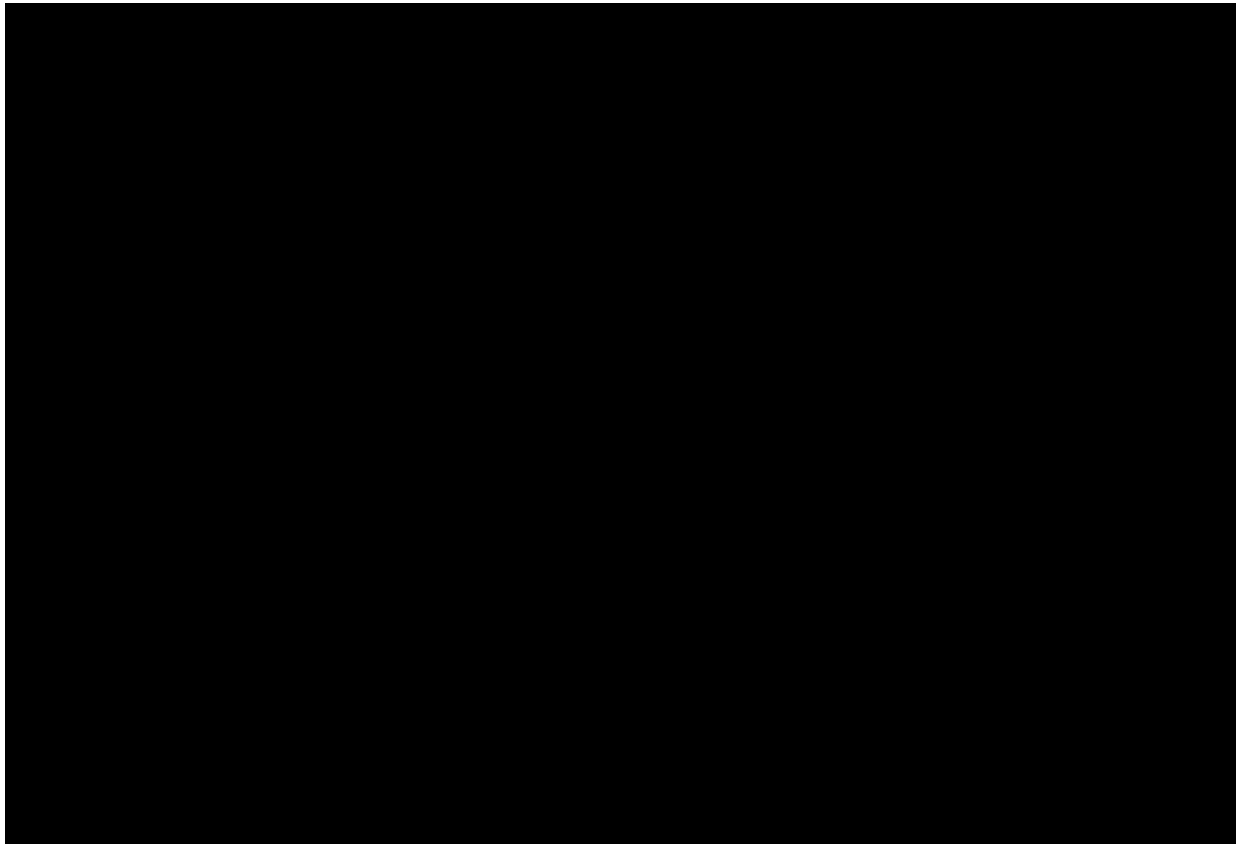
687. [REDACTED]

[REDACTED]

[REDACTED]

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<sup>816</sup> DeJohn deposition 6/17/16 p. 44-53, L. 18-7



**B. Bard Marketing needed a new retrievable and permanent IVC filter to grow its IVC filter business.**

688. In 2004, the Recovery Filter's Brochure indicated that Bard had established itself as an innovator and leader in the vena cava world, leveraging its decade-long experience (with SNF) to bring the physician the "next generation in filter performance." Bard's marketing to physicians represented that the Recovery was a "marked improvement" in performance over other available filters (including the predicate SNF):

*Introducing RECOVERY. A marked improvement over currently available devices. Recovery's filter's unique self-centering design, proven conical shape and bi-level filtering system create the ideal balance between clot trapping efficiency and caval patency.*

**CLOT TRAPPING & CAVAL PATENCY-** *-system effectively traps large and small emboli without compromising caval patency*

**LOW PROFILE**

**SELF-CENTERING-** *promote a centered placement*

**SECURE FIXATION-** *The filter hooks are loaded into a delivery system that is specifically constructed to prevent leg crossing.*

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<sup>817</sup> DeJohn Exhibit 355; DeJohn deposition 7/18/16, p. 53-64, L. 8-9

***LATEST ADVANCE IN FILTER TECHNOLOGY-** incorporates the best feature of today's most advanced caval filtration devices while overcoming the disadvantages associated with older designs.<sup>818</sup>*

689. These marketing materials did not inform physicians of any of the safety issues occurring with the RNF, nor that Bard had itself silently discontinued marketing its Recovery filter in September 2005.

**C. Bard's aggressive marketing was able to overcome negative clinical experience and an absence of solid clinical data.**

690.

[REDACTED]

691. Mr. DeLeon explained the role of the Bard sales force for reporting complaints, "*our role was to report complications, and then other teams took it from there.*" He continued, "*The sales team was pretty much instructed on how to report those complaints. Where they went from there, sir, I have no idea.*"<sup>821</sup>

692.

[REDACTED]

693.

[REDACTED]

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<sup>818</sup> BPV-17-01-00007760.

<sup>819</sup> DeLeon deposition 6/16/16, p. 50, L. 6-13

<sup>820</sup> DeLeon deposition 6/16/16, p. 29-34, L. 4-3

<sup>821</sup> DeLeon deposition 6/16/16, p. 29-30, L. 11-9

<sup>822</sup> DeLeon deposition 6/16/16, p. 34, L. 4-24

<sup>823</sup> DeLeon deposition 6/16/16, p. 42-43, L. 11-1

694. With regard to developing annual quotas, Mr. DeLeon said that “a revenue goal was given to [him] as a district manager, and then [he] had the ability to divide up the revenue goals for each individual territory manager ... as [his] discretion based on size of opportunities” and sales experience. He testified that “quotas, sales targets, sales goals [and] revenue goals” are synonymous.<sup>825</sup>

695. [REDACTED]

696. [REDACTED]

697. [REDACTED]

698. [REDACTED]

699. Cook’s Gunther Tulip had been available as a removable filter in Canada. It was known to Dr. Asch at time of his RNF study. In the United States it was originally cleared as a permanent IVC Filter on October 18, 2000, two years before the RNF. It would be cleared as a permanent filter with a retrieval option at 14 days and its Retrieval Set on October 31, 2003. At the time of the POA for RNF there was no FDA cleared retrievable filter. The Gunther Tulip was being removed off-label at 14 days. The Cordis OptEase in Europe was removed at 12 days. [REDACTED]

<sup>824</sup> DeLeon deposition 6/16/16, p. 57-59, L. 19-21

<sup>825</sup> DeLeon deposition 6/16/16, p. 52-53, L. 21-10

<sup>826</sup> DeJohn deposition 6/17/16, p. 132-137, L. 15-25

<sup>827</sup> BPV-17-01-00030248 in BPV-17-01-00030232

<sup>828</sup> BPV-17-01-00030248 in BPV-17-01-00030232

<sup>829</sup> BPV-17-01-00030248 in BPV-17-01-00030232

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<sup>832</sup> BPV-17-01-00030248 in BPV-17-01-00030232

[REDACTED]

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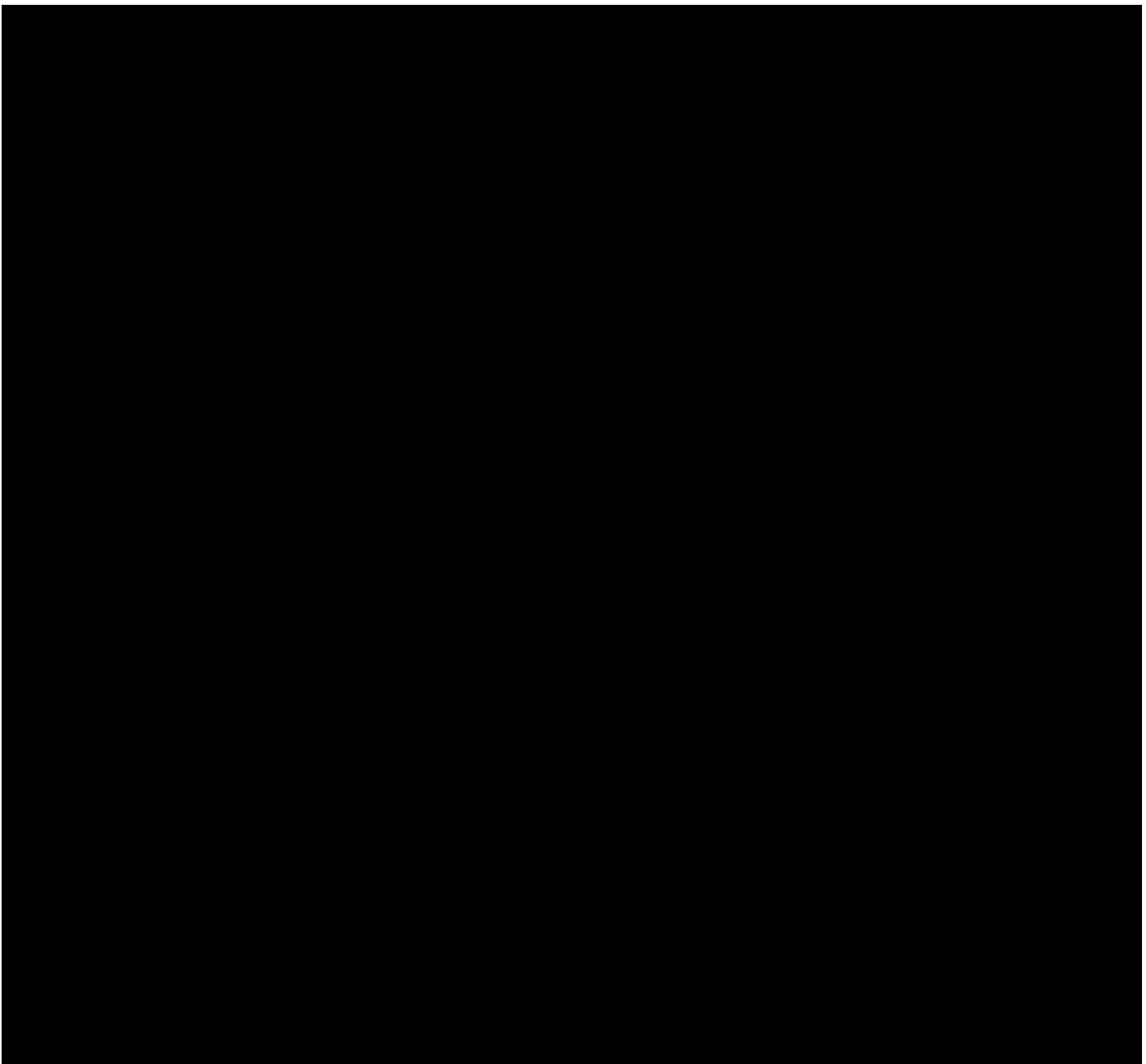
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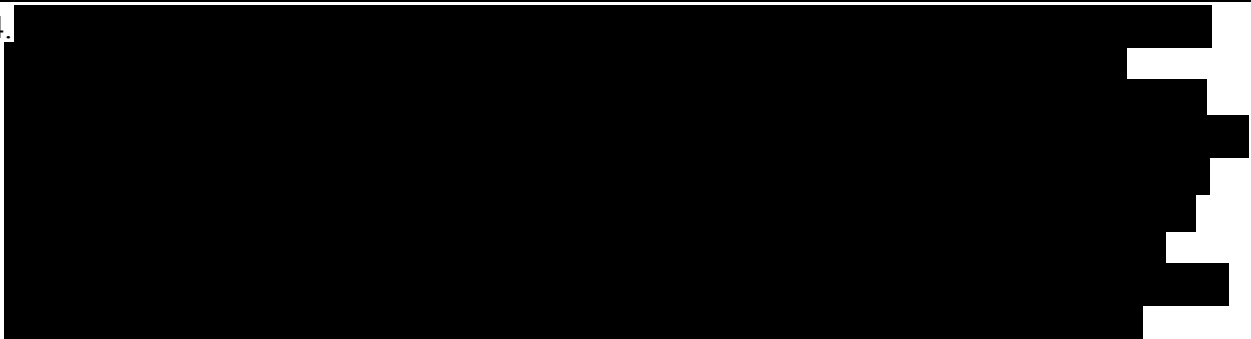
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<sup>833</sup> BPV-17-01-00030248 in BPV-17-01-00030232

<sup>834</sup> DeJohn Exhibit 336



704.



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<sup>835</sup> DeJohn Exhibit 336

705. [REDACTED] ters.

[REDACTED]

706. [REDACTED]

707. [REDACTED]

708. [REDACTED]

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710. [REDACTED]

[REDACTED]

[REDACTED]



711.



712. Dr. Grassi was asked in 2014 about the Recovery and G2 Filter IFU from 2002 through 2008 (Grassi Exhibits 133, 133, 134, 136, 137, 138), with a Dear Doctor letter attached to the December 2004 label exhibit in the letter or the Potential Complications or elsewhere in any of the labels the physicians were advised that filter ‘tilt’ could occur after placement of the filter. His response was that under Potential Complications the IFUs referred to migration or movement of the filter device rather than tilt.<sup>842</sup>

*Q. ...Well, I was just going to ask you, do you consider a filter that tilts after it's properly placed into position a migration?*

*A. No, I would consider a tilt to be more of a form of relative movement of the filter device, or at least a shift in its orientation with respect to the center axis of the inferior vena cava*

*Q. How would you define migration?*

*A. I would define migration as a clinically significant movement, and usually in the literature it is defined as movements that are sizeable, that is greater than 2 cm and frequently many, many centimeters.<sup>843</sup>*

713. Dr. Grassi was then asked about same series of IFUs for Recovery and G2 from 2002 through 2008 and under “Potential Complications” or “Precautions” or elsewhere did any IFU tell physicians that after placement, proper placement of the filter, there may be inability to remove it. He responded after looking at the IFUs:

*What I can say and what I do see is that there are precautions and technical instructions, a label, talking about the proper way to insert as well as the proper way to remove the filter, but I don't immediately see the phrase which you just mentioned.<sup>844</sup>*

714. Dr. Grassi was then asked about the labels from 2002 through 2008 and the risk for a need for open surgery to remove either the Recovery or G2 Filters:

*Q. Another question I have is, with regard to tilt or inability to remove, is there anything in these Instructions for Use that advise the doctors*

<sup>841</sup> BPV-17-01-00120487; Phase 0 Design review; G1A Recovery Filter [BPV-17-01-0012189]

<sup>842</sup> Grassi deposition 8/27/14, p. 464-467, L. 8-17

<sup>843</sup> Grassi deposition 8/27/14, p.467-8, L. 18-8

<sup>844</sup> Grassi deposition 8/27/14, p. 468-9, L. 13-3

*that they may need to undergo or have the patient undergo an open procedure to remove the temporary filter?*

*A. By looking at these IFUs, from what I can determine on this viewing, I don't see that specific language.<sup>845</sup>*

**E. Bard's publication of Dr. Asch's RNF retrieval data encouraged un-cleared, off-label, temporary use.**

715. Bard sponsored Dr. Asch's study in Toronto, CA. It was involved throughout the entire process of the case series of 32 patients developed by Dr. Asch. This paper is published in *Radiology* on December 2002, clearly discussing the benefits of Bard's Recovery IVC Filter for Retrieval. There is no disclaimer to inform United States physicians that it is not cleared for retrieval in the United States. RNF retrieval is an investigational use and requires the patient to be enrolled in an FDA approved Investigational Device Exemption (IDE) with monitoring, oversight, periodic reporting and adequate informed consent. The Asch abstract was first submitted to *Radiology* on November 14, 2001 with revisions made through June 26 2002 when it was accepted. It was available on-line prior to publication.<sup>846</sup>

716. The article fails to discuss the failure investigation of the filter migration for Patient# 9. The rationale for the migration was that the RNF filter was overwhelmed by a large clot. However, IVC Filters are intended to capture and hold clots.

717. Dr. Asch wrote about the 'medical need' for the availability of retrievable filters. He described that the Gunther Tulip<sup>847</sup> was a permanent and retrievable filter already available in Canada since March 1998. The Canadian IR Registry's description of the complications of the Gunther Tulip Retrievable Filter, further support the need for a new alternative retrievable filter that could allow the filter to be retrieved at periods greater than 15 days. Dr. Asch indicated one patient had retrieval at 134 days (although there was no indication given that this was the patient with the Recovery filter arms seen perforating outside the vena cava). Dr. Asch reportedly wrote that there was "no upper limit for retrieval time with the current RNF design." He continued,

*The medical need for a retrievable filter design is demonstrated by the off-label use of currently approved permanent filters...*

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<sup>845</sup> Grassi deposition 8/27/14, p. 469, L. 13-21

<sup>846</sup> Dec. 2002; 225(3):835-44 (DOI:10.1148/radiol.2252011825)

<sup>847</sup> Gunther Tulip was cleared as K000855 for Cook as a permanent IVCF in October 18, 2000. It was submitted for marketing on March 16, 2000. "Gunther Tulip Vena Cava and Retrieval Set" was cleared as K032426 on October 31, 2003. Unlike the RNF, the Tulip was cleared along with its retrieval, set which was cleared as designed for removal of the Gunther Tulip. Cook provided FDA with a clinical study in 41 patients, with 15 patients not retrieved. Results from the clinical study showed that the filter could be safely retrieved.

*...A more common indication for filter removal is filter migration, either occurring at the time of implantation or seen at follow-up. Perhaps less common is filter infection...*

*The Gunther Tulip filter was approved for both permanent placement and retrieval in Canada in March 1998. In the United States, it is approved for permanent use. Recently published data from the registry of the Canadian Interventional Radiology Association regarding the placement of 91 Gunther Tulip filters currently represent the most extensive experience with the device...Fifty-two were successfully removed at a mean of 9 days after placement. ...These results support the need for a filter than can be removed well beyond the 10-15 day window.*

*...Filter design is also import...the design of the RF allows for the filter arms to slide out of any potential sleeve once the elastic leg hooks have been removed from the caval wall. The animal data demonstrating the ability to remove an RNF at 22 weeks, coupled with the fact that one was removed from a human at 134 days, suggest that there is no upper limit to the time of retrieval with the current design. In contrast, studies of virtually all other filter designs included cases in which the filter could not be removed 2 weeks after insertion...*

718. Rather than using other percutaneous tools used “off-label” for filter removal, Dr. Asch described Bard’s Recovery Cone as intended for removal of the RNF. He describes during the clinical study difficult filter retrievals with moderate angulation, tilting as well as his learning curve:

*In spite of moderate angulation in several cases in the series, all filters were easily and successfully retrieved.*

*...As our experience grew, changes in technique occurred.*

719. In the Asch study the author indicated that 32 patients were implanted in his trial with the Recovery Filter, with removal in 24 patients, and three patients dying of non-related causes. The article was published in Radiology on December 2002. The RNF was placed for a prophylaxis indication (N= 2 patients). The mean implantation time for the RNF was 53 days (*range 5-134 days*). Trapped thrombus was seen in the filter in seven cases. In one patient with a large thrombus, the filter was noted to have migrated 4 cm cephalad (Patient #9). According to Dr. Asch, the study demonstrated the feasibility and safety of retrieval up to 134 days after implantation (Patient with the RNF arms outside the vena cava on imaging).

720. Dr. Asch made the distinction in 2002 between temporary filters and retrievable filters. A “temporary filter” was a filter attached to some form of tether, such as a guide wire or catheter, and thus must be removed. The anchoring mechanism resulted in the patient having to be immobilized and may serve as a nidus for infection. In contrast, he called a “retrievable filter” as able to be left in place permanently or retrieved, depending on the clinical situation. At the time

of his study with the RNF the Gunther Tulip Filter (Cook Canada) was already available as a “retrievable filter.”

721. Asch referenced Lorch (2000),<sup>848</sup> a review of data from a multicenter registry, it was concluded that filters can be retrieved or left in place at the option of the physician would be an appropriate kind of temporary filter to use as long as the retrieval procedure was technically easy and had a low complication rate. There is no mention that the device when left implanted in patients should be able to perform as a safe and effective permanent filter. If it cannot be permanently implanted, the physician selecting the device to implant must receive adequate instructions about the anticipated life expectancy of the device implanted in a patient and a warning for both the patient and the physicians about the need for monitoring for risks if the device is left implanted.

722. The Asch study examined all patient images for tilt, migration, trapped thrombus and caval perforation. He indicated one filter was placed in a patient with a vena cava 33mm. There is no mention in the Asch study of the patient (#33) receiving the RNF prophylactically during pregnancy and her subsequent filter fracture and the change to the instructions for use based on her filter fracture.

723. The Asch study has the following “Acknowledgements” regarding the involvement of the Defendant in the publication:

*The author gratefully acknowledges Rob Carr, BSc, Paul Stagg, BA and Monica Coutanache, RN for ongoing assistance during the study. Special thanks also to John Kaufman, MD, and Rob Carr for manuscript review.*<sup>849</sup>

724. There does not appear to be anything in the acknowledgement that discloses that the people being cited by Dr. Asch for “ongoing assistance” are Bard employees and a key Bard consultant.

725. When the finding of the patient at 134 days with several of the Recovery filter arms outside the vena cava is added to the migration patient #9 investigated in 2000 and the fracture issue in patient #33, not in the published paper, the Defendant had sufficient notice by 2002 that the RNF and the SNF were not substantially equivalent. The RNF had serious design flaws that significantly impacted even its short-term performance as an implanted filter at less than 134 days. The Defendant was able to obtain FDA clearance describing the device it intended to sell, a RNF that when used as a “permanent filter” was substantially equivalent which is equal or better to the predicate SNF. The Defendant had signs that the Recovery as designed and produced was worse than the SNF before it was even launched for use as a permanent filter. It was ultimately Defendant’s responsibility to ensure that the Recovery Filter it sold in the United States was substantially equivalent to the predicate SNF filter and performed as described to the FDA in its cleared 510(k). To market a device that did not perform as 510(K) cleared and described to the

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<sup>848</sup> Lorch H, Welger D, Wagner V, et al., Current practice in temporary vena cava filter insertion: a multicenter registry, *J. Vasc. Inter. Radiol.*, 2000, Vol. 11, at 83-88

<sup>849</sup> Asch (2002).

FDA, namely substantially equivalent to the SNF when used as “permanent filter” was to market an adulterated class III device that did not have pre-market clearance.

726. As a result of the pregnancy and a fractured arm and embedded hook for Patient 33, the FDA was told—but Interventional Radiologists were not told—that a precaution was added to the Instruction for Use which stated that a suprarenal position for filter placement should be used in a women who is pregnant or of childbearing age.<sup>850</sup> This statement was added “as suggested” by the American College of Radiology “Standard Performance of Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism,” effective January 2001.

**F. Bard’s KOL Dr. Binkert helped support “long indwell time” for G2 filter retrieval.**

*There is concern in the medical community that IVC Filters, although effective at preventing recurrent PE in the short term, could increase the risk of later DVT or vena cava thrombosis (Decousus et al. NEJM, Dec 1998). In the EVEREST study, the mean indwell time for retrieved filters was 140 days (median 144 days, range 5-300 days). This represents the greatest “window” of retrievability than that for competitive devices. The Gunther Tulip Filter (Cook) reports a mean indwell time of 11 days (range 2-20 days) in their IFU. Similarly, the OptEase Filter’s IFU states a mean dwell time of 11 days (range 2-14 days). Extending optional IVC filter use beyond several weeks could allow later filter retrieval in patients who might benefit from longer PE prophylaxis. Longer indwell times would also allow postponing the retrieval procedure in patients who were unsuitable because of such conditions as the presence of a C-collar for cervical spine injury. Ideally, an optional filter should be able to be retrieved at any time when clinically indicated without the need for repositions.<sup>851</sup>*

727. Bard’s marketing promoted IVC filters for permanent use in morbidly obese patients with the “longest window of retrieval” to physicians. But Bard failed to adequately disclose to physicians the increased risks for implanted morbidly obese patients, including the increased retrieval difficulties, need for additional surgery, and increased risks of clotting, filter fractures, migration of fragments to the heart and bleeding associated with longer filter indwell time.<sup>852</sup>

728. Bard’s Recovery IVC Filter U.S. Launch Update of November 17, 2003, was to provide financial support for clinical programs and sell sheets for marketing designed to promote (expand) filter use for wider types of specialties.

729. Bard’s internal IVC filter marketing plans proposed that Bard provide financial support for 30 patient studies conducted in diverse areas of bariatric, orthopedic surgery and trauma surgery. But

<sup>850</sup> Notably, however, Defendant’s Instructions for Use did not warn that the RNF could fracture, or that the filter could migrate caused by something other than physician error.

<sup>851</sup> Binkert (2006)

<sup>852</sup> Cheung MC, Asch MR, Gandhi S, Kingdom JCP, Temporary inferior vena caval filter use in pregnancy, *J Thromb Haemost* 2005, Vol. 3, at 1096-97; Asch (2002)

the rationale for Bard's study funding was not safety but rather to sell more filters. Each Bard-funded study reportedly would influence twenty people to buy Bard IVC filters.

730. Bard marketed its modified RNF sold as the G2 filter as a "permanent filter" with new and unsupported claims of "Improved Centering," "increased" migration resistance, "enhanced" fracture resistance, and as a "brand new filter platform taking strength and stability to a new level." The marketing implied to a physician that this was a newer device than the RNF. The 510(k) cleared the G2 as a modification of the RNF therefore, substantially equivalent to the RNF which was substantially equivalent to the SNF as a permanent filter. This was not supported in Bard's Product Performance Specification (PPS070028) testing of migration resistance to the SNF when Bard had to change the specification to the RNF when it failed to match performance of the SNF.<sup>853</sup>

731. Bard was implying new unsupported performance claims for the G2 filter that it had already made as unsupported claims in the RNF 2004 brochure. Prior RNF claims such as self-centering, migration resistance and stability, effective clot-trapping.<sup>854</sup>

[REDACTED]

732.

[REDACTED]

[REDACTED]

733.

[REDACTED]

734.

[REDACTED]

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<sup>853</sup> BPVE-01-00272936

<sup>854</sup> BPV-17-01-00007760

<sup>855</sup> DeJohn Exhibit 344

<sup>856</sup> DeJohn Exhibit 340, BPV-01-00492576; DeJohn Exhibit 348

<sup>857</sup> DeJohn deposition 7/18/16. p. 146-153, L. 1-6

[REDACTED]

735. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

736. [REDACTED]

737. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

738. [REDACTED]

739. [REDACTED]

740. [REDACTED]

741. [REDACTED]

742. [REDACTED]

[REDACTED]

[REDACTED]

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[REDACTED]

[REDACTED]

743. [REDACTED]

744. [REDACTED]

745. [REDACTED]

[REDACTED]

746. [REDACTED]

[REDACTED]

Use of the OptEase Filter and for the OptEase Retrieval Catheter. The OptEase Retrieval Catheter was cleared by FDA for removal of the OptEase Filter only by a femoral approach. Cordis' 510(k) K034050 cleared May 22, 2004 included Defendant's recovery Filter System as one of several removable option filter predicates.

747. Bard's last Recovery 510(k) clearance, the "Recovery G2 Filter System- Femoral Delivery" does not include a request for clearance or a mention of the Recovery Retrieval Cone. The FDA's clearance refers a reader to look at the "Instructions supplied under the section labeled: Optional Procedure for Filter Removal." (K073090- cleared January 15, 2008) was the first FDA clearance of a Recovery G2 since the initial Recovery was cleared as a "retrievable" option system in 2003. Up until 2008, no "Recovery G2 Filter" other than the Recovery RF-048f was cleared by FDA to be "legally marketed or promoted as a retrievable filter." In fact, the G2 was required to carry a Precaution warning *against* retrievable/temporary use.

**C. Bard's Draft Recovery Cone handle detachment investigation described no plan to recall a defective device from the U.S. market.**

748. There is a draft Subject Product Analysis Approval Sheet for Bard Recovery Cone Removal System Handle Detachment SPA #08-04-01 Rev. 0. In 2007, BPV had experienced an increased rate of handle detachment complaints compared to the prior years.



### 3.1 Customer Complaints

A total number of Recovery Cone Removal System handle detachment complaints, received by BPV between March 2004 and March 2008, is twenty-four (24). The summary of Recovery Cone Removal System handle detachment complaints is as follows:

YEAR	NUMBER OF UNITS DISTRIBUTED	NUMBER OF COMPLAINTS RECEIVED	COMPLAINT RATE %
2004	3,082	0	0
2005	3,895	3	0.08
2006	3,866	2	0.05
2007	4,217	15	0.36
2008	1,064	4	0.38
Total	16,124	24	0.15

All Recovery Cone Removal System handle detachment complaints received to date represented RC-15 products. There have been no customer complaints reported to date for FBRC handle detachment issues.

The FBRC product is commercially available since January 2008. It is identical to RC-15 product in design, material composition, and manufacturing process. The FBRC products have an additional (foreign body removal) indication, which is reflected on FBRC labeling.

868

749. The Recovery Cone handle detachments were occurring with the RC-15 products. There had been eight (8) complaints filed as MDRs. Two (2) were classified as patient injuries. One of the events (complaint 143941-October 8, 2007) required a cut down on the introducer sheath to remove the cone system and an intervention through a second percutaneous access site (femoral) to retrieve the filter with a snare. In the second event (complaint 156840- January 18, 2008), a surgical cut down was required to remove the detached portion of the device. Six (6) other MDRs were classified as malfunctions that resulted in “user dissatisfaction issues.”<sup>869</sup>

750. The HHE was approved by Bard’s Medical Consultant on April 15, 2008. The overall severity of risk was determined to be Moderate. The root cause conclusion was “*most probable - variation in the Lap Welder temperature control, as a result of intermittent connections at the contacts where the temperature controllers are installed.*” The post-proof inventory – RC-15 205 Recovery Cone inventory, FBRC 235 Recovery Cone inventory as of April 15, 2008. The

<sup>868</sup> BPVE-01-00986615

<sup>869</sup> BPVE-01-00986615

calculated complaint rate for 2007/2008 is 0.36%. 1000 units were produced prior to implementation of manufacturing change (100% in-process proof load test).

751. The Recovery Cone Removal System is the only product indicated for removal of the RNF and G2 filters. Field correction risk would be a physician not having the product available for removal of the RNF or G2 filter. Another risk is that the physician without a Recovery Cone will use a snare (off-label) to remove the RNF or G2 filter. The IFU indicates that use of other devices can lead to filter malfunction and serious patient complications such as perforation, migration, fracture, tilting, pulmonary emboli. A third risk is that the patient does not have a planned filter retrieval and is “lost to follow-up” and risk of a permanent IVC Filter. According to Bard, these risks were considered greater than the risk of a handle detachment.
752. Bard concluded that “based on the risks, the potential risks of a filed correction outweigh the benefits.” Therefore, Bard took no action to remove the defective Recovery Cone removal Devices from the market or to notify physicians of the risk for the handle to detach.

The following table summarizes the units and lots involved in this investigation:

PRODUCT CODE	NUMBER OF LOTS	QUANTITY	RANGE OF MANUFACTURING DATES
RC-15	400	12,203	4/1/05 – 4/1/08
FBRC	47	1,483	1/10/08 – 4/9/08

See Appendix 7 for a complete listing of the Recovery Cone units and lots involved in this investigation.

870

753. The United States with 11,113 RC-15 and 828 FBRC had the greatest number of defective Recovery Cone units compared to the rest of the world. Bard at the time of the Draft document did not voluntarily plan to recall (21 CFR 806) any of the known defective lots of Recovery Cone RC-15 from the United States.<sup>871</sup>

**D. Bard finds “no root cause” acceptable for investigation of Recovery Cone marker band movement & detachment.**

754. Bard has a November 2009 Recovery Cone Marker Band Movement or Detachment SPA 09-07-02 Rev.1 signed by Gin Schulz, Division Head of Quality.<sup>872</sup>

<sup>870</sup> BPVE-01-00986615

<sup>871</sup> BPVE-01-00986615

<sup>872</sup> BPV-17-01-00144921

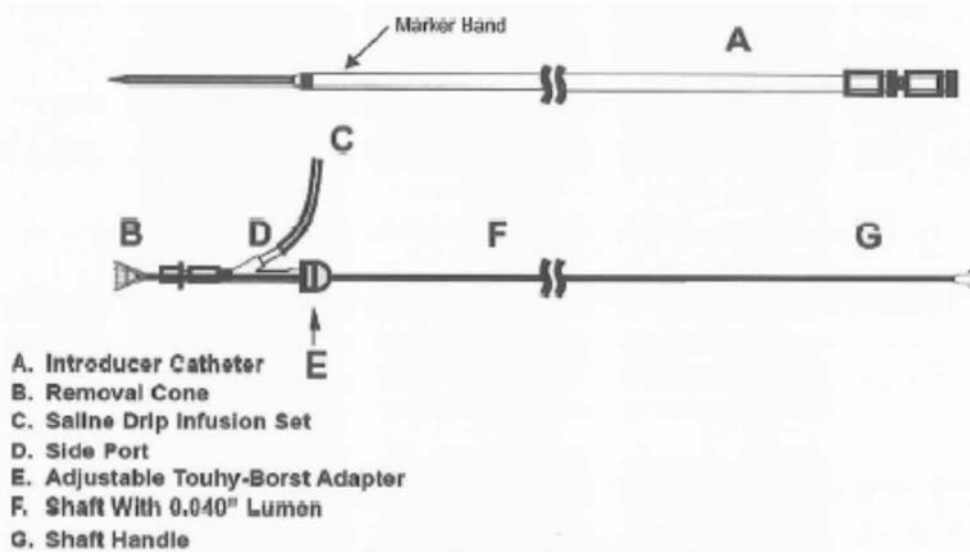


Figure 1. Recovery Cone Removal System

Product Code	Product Description	Production Distribution
RC-15	Recovery Cone Removal System	US (prior to 1/2008) OUS
FBRC	Foreign Body Recovery Cone Removal System	US (after 1/2008)

Table 1. Availability and Distribution of Recovery Cone Removal System

#### 0 DESCRIPTION OF PROBLEM (DEFINE)

An increased rate of complaints for migration (movement/detachment) of the radiopaque markerband was detected by Bard in July 2008. The majority of cases reported a movement of the band from the swaged location, at the distal end of the Recovery sheath, proximally up the sheath. A minority of cases reported a distal movement of the band, resulting in a detachment of the band from the sheath.

Table 2 summarizes the complaint rate for marker band movement/detachment by year (Ref. Appendix 7 for detailed descriptions of the complaints):

Year	# of Units Distributed	# of Complaints Reported	Complaint Rate (%)
2004	2648	4	0.15
2005	3895	9	0.23
2006	3866	3	0.08
2007	4217	2	0.02
2008	3353	14	0.41
2009*	4069	19	0.47

Table 2. Complaint Rate

\*2009 data covers up to 9/30/09.

873 BPV-17-01-00144921

874 BPV-17-01-00144921

875 BPV-17-01-00144921

755. Bard had received a number of complaints of the marker moving or detaching from the Recovery Cone since July 2008 through September 2009.

756. There was an HHE performed by Dr. Altonaga, a Bard Medical consultant on July 23, 2009.

*“The HHE indicates that the overall severity of risk associated with the reported RO marker band issue is most likely to represent a varying degree of morbidity and less likely mortality.”* For distal attachment of the marker band (minority of cases) the severity was determined to be Moderate, a failure that may cause a moderate injury to the user or patient, but *“will not result in death.”* The injury does require treatment.<sup>876</sup>

757. GFO implemented an investigation in Q4 2008 (GF 08-013, Rev 0) to evaluate the potential manufacturing causes. After reviewing and analyzing all information, a clear root cause was not found. However, GFO made improvements to the swaging process.<sup>877</sup>

**E. FDA’s 2015 warning letter indicated that Bard required clearance of the Recovery Cone removal system.**

758. The FDA’s July 13, 2015 Warning Letter classified the Recovery Cone Removal System not as a Class I manual surgical snare exempted from premarket notification. FDA classified the recovery Removal Cone, Model FBRC as a percutaneous retrieval system “which is a manual instrument intended for specialized use within a specific medical specialty, cardiovascular surgery, the Recovery Cone Removal Systems, Model FBRC is specialized intended sue for removal of inferior vena cava filters, specifically Bard’s G2X, G2 Express, and G2 filters. Bard was told by FDA to immediately cease activities that resulted in the misbranding and adulteration of the Recovery Come Removal System, Model RC-15 and Recovery Cone Removal System, Model FBRC.

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<sup>876</sup> BPV-17-01-00144921

<sup>877</sup> *Id.*



APPENDIX A  
**SUZANNE PARISIAN, M.D.**  
**CURRICULUM VITAE**

**EMPLOYMENT HISTORY:**

**8/95-        PRESIDENT**  
**MD ASSIST, Inc.**  
7117 N. 3<sup>rd</sup> Street  
Phoenix, Arizona 85020

**12/1993-7/95 CHIEF MEDICAL OFFICER**  
Division of Reproductive, Abdominal, Ear, Nose and  
Throat, and Radiology (DRAERD)  
OFFICE OF DEVICE EVALUATION (ODE)  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)  
FOOD AND DRUG ADMINISTRATION (FDA)

**8/1991-7/95 Lt. Commander**  
United States Public Health Service

**8/1991-3/1993 Medical Officer**  
Office of Health Affairs (OHA)  
Center for Devices and Radiological Health (CDRH)  
FOOD AND DRUG ADMINISTRATION (FDA)

**4/1993-11/93 Medical Officer**  
Division of Reproductive, Abdominal, Ear, Nose &  
Throat, and Radiology (DRAERD)  
Office of Device Evaluation (ODE)  
Center for Devices and Radiological Health (CDRH)  
Food and Drug Administration (FDA)

**8/1991-7/95 Clinical Staff Appointment**

Office of the Medical Examiners for Armed Forces  
Armed Forces Institute of Pathology (AFIP)  
Washington, D.C.

**4/1985-6/1987 General Practice**

AVTEX Fibers, INC  
Front Royal, Virginia

**4/1980-7/1981 Emergency Medicine**

President  
Mountain Emergency Medical  
Caldwell Memorial Hospital  
Lenoir, North Carolina

**10/1979-3/1980 General Practice**

Caldwell County Health Department  
Lenoir, North Carolina

**CDRH / FDA /HHS & USPHS HONORS:**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Employee of the Month** August 1993

**FOOD AND DRUG ADMINISTRATION**

**Employee of the Month** August 1993

**CENTER FOR DEVICES AND RADIOLOGICAL HEALTH**

**Employee of the Month** August 1993

**Public Health Service's Achievement Medal- 1992**

**Public Health Service's Unit Commendation Medals**

Acupuncture Workshop- 1995  
Total Parenteral Nutrition Complications Group- 1995  
Night Vision Equipment Radiation Leak Group- 1995  
Anesthesia Heated Wire Circuit-1994  
Small-Bore Anesthesia Group-1992  
Corporate-Wide Injunctions Groups-1993, 1994, 1995

**Public Health Service's Commendation Medal**

Neonatal Ventilators-1992  
Hemodialyzer Reuse Labeling-1995

**Public Health Service's Unit Citations- 1992, 1992**

Latex Allergy-1993

**Nominee for FDA Honor Award**

FDA's Policy for Hyperthermia Clinical Trials-1995

**Certificate of Appreciation CDRH's Staff College**

Clinical Trials Course, Spring, 1995

**Other Honors**

University of Central Florida, *Cum Laude*, 1974

University of Central Florida, *Summa Cum Laude*, 1975

**REGULATORY ACTIVITIES:**

**OFFICE OF DEVICE EVALUATION (ODE) PRIMARY RESPONSIBILITY:**

**Primary responsibilities included:**

- 1) Review of FDA Premarket applications-**  
510Ks, Investigational Device Exemption (IDEs), Premarket Approval Applications (PMAs)) including design, labeling, health issues and quality systems requirements for manufacturing issues; INDs.
- 2) Review and evaluation of clinical trials, etc;**
- 3) Design of Post Marketing Clinical Studies;**
- 4) Health Risk Assessments and management for Office of Compliance and the FDA District Field Offices;**
- 5) Liaison for manufacturers, clinical investigators, government agencies, medical community, press, Congress, patient advocate groups, public, and manufacturers organizations;**
- 6) Training of ODE clinical reviewers;**
- 7) Quality Assurance design;**
- 8) Identification and resolution of safety and efficacy issues;**
- 9) Presentation of clinical device issues to FDA Advisory Panels;**
- 10) Presentation of Device-related issues to Health Care Financing Administration's Technology Assessment Committee (HCFA, TAC);**
- 11) Investigator and Manufacturer Guidances from CDRH for Clinical Protocols;**

**12) Clinical support for FDA regulatory actions and hearings.**

**CLINICAL DEVICE RESPONSIBILITY AREAS in ODE:**

**ENT** - Cochlear implants, brainstem implants;

**Radiology** - Magnetic Resonance Imaging, Ultrasonography, Mammography, Radiation Hyperthermia Therapy, Neurosurgical Imaging Systems, Interventional Radiology, Thermography, Radiotherapy;

**Urology**- cryosurgery, lasers, stents, penile prostheses, urethral implants, lithotripsy;

**Extracorporeal circulation** - Hemodialysis, LDL-Apheresis, Plasmapheresis, Immunadsorption, Cell Harvest; Organ Preservation;

**Pulmonary**- bronchoscopy, stents;

**Gynecology**- infertility, PAP smear technology;

**Obstetrics**- chorionic villus sampling, amniocentesis, fetal monitoring;

**Gastroenterology**- biliary stents, neuromuscular stimulators;

**Endoscopy & Laparoscopy; Lasers;**

**Alternative Medicine for FDA;**

**Immunology;**

**In vitro diagnostics; Toxicology; Cytology;**

**Biological Artificial Organ Assist Devices (Center for Biologics Evaluation and Review (CBER);**

**Implanted Neuroelectrical Stimulators;**

**Genetics; Perinatology;**

**Transfusion Medicine; Electromagnetic Fields and Interference;**

**Tissue and Organ Transplantation (CBER);**

**Forensics**

**Combination Products-Drug/Device, Biologics/Device**

**Contrast Agents**

***100 Health Risk Assessments while in ODE***

**OFFICE OF HEALTH AFFAIRS PRIMARY RESPONSIBILITY :**

**1) Primary support for Office of Compliance-**

Health Risk Assessments & Health Hazard

Evaluations; review of Labeling, Mandatory Device Reports (MDRs), Adverse Experience Reports (AERs)

2) Interaction with manufacturers, investigators, health care providers, professional organizations;

3) Interaction with FDA District Offices, other government agencies, the Office of Device Evaluation;

4) Identification of public health and safety issues.

**Primary Clinical Responsibility Areas for OHA:**

Cardiovascular; Anesthesia; Pulmonary;  
Orthopedics; Unconventional Therapies;  
Rehabilitative Medicine; Pathology; Home Health;  
Emergency Medicine; Hemodialysis; Toxicology; Radiology

***162 Health Risk Assessments while in OHA***

**FORENSIC MEDICINE CLINICAL ACTIVITIES:**

Evaluation of Patient Cause of Death & Injury with FDA-Regulated Products  
Review and Final Sign-Out Cause of Death Military, Dependent,  
FBI and CIA  
Armed Forces Institute of Pathology  
Office of Medical Examiner  
Washington, D.C.

**Center for Devices and Radiological Health (CDRH) Assigned Support:**

Anesthesia Post Market Surveillance Chairman (1992- May, 1993)  
FDA and CDRH's Liaison for Alternative Medicine  
CDRH Staff College Instructor, Clinical Trials  
Temple Tier II Report-ODE's Internal Quality Assurance (QA) Review

**CDRH's Representative**

National Kidney and Urological Diseases Advisory Board  
National Institutes of Health  
Health Care Financing Administration's Technology Assessment Committee  
Ad Hoc Working Group CDRH Transfusion Medicine

**CDRH's Support for FDA's Office of Legislative Affairs (OLA) and Press Office for:**

Extracorporeal Hyperthermia and treatment of patients with AIDS;  
Alternative Medicine;  
Hemodialysis

**LECTURES While at FDA:**

Armed Forces Institute of Pathology  
Essentials of Medical Devices and Death Investigations  
Washington, D.C.  
**October, 1993**

Third World Conference of Acupuncture  
FDA's Viewpoint of Acupuncture  
Kyoto, Japan  
**November, 1993**

Alternative Medicine Conference  
FDA's Viewpoint of Acupuncture  
Smithsonian Museum of Medicine  
National Museum of Medicine  
Washington, D.C.  
**December, 1993**

Reuse of Hemodialyzers  
Office of Device Evaluation  
Presentation and Review of CDRH's Draft Guidance Document  
Rockville, Maryland  
**December, 1993**

Panel Chairman  
Office of Alternative Medicine/National Institutes of Health (OAM/NIH)  
Workshop for Acupuncture Needle Reclassification  
Provided FDA's Viewpoint  
Rockville, Maryland  
**April, 1994**

National Acupuncture and Oriental Medicine Alliance  
Annual Conference  
FDA's Viewpoint - Acupuncture  
Crystal City, Virginia  
**May, 1994**

OAM/NIH and FDA's Workshop Planning Group  
for Herbs Conference,  
FDA's and CDRH's policy  
For Alternative Medicine Providers  
Rockville, Maryland  
**May, 1994**

American Association for Medical Instrumentation (AAMI)  
FDA's perspective Hemodialysis Reuse Labeling Guidance  
Washington, D.C.  
**June, 1994**

AAMI Conference  
FDA's Recommendation for Hemodialyzer Reprocessing Labeling  
Hemodialysis Reuse Section  
Washington, D.C.

**June, 1994, November 15, 1994  
& May 9, 1995** (Joint AAMI/HIMA Workshop)

FDA's Genitourinary Advisory Panel  
Presentation Hemodialysis Reuse Labeling Guidance  
Rockville, Maryland  
**July, 1994 & January 1995**

FDA Urology Devices Advisory Panel Meeting  
Presentation of LDL-Apheresis Premarket Applications  
Kaneka's Liposorber LA-15 System  
B. Braun of America's H.E.L.P. System  
Rockville, Maryland  
**April, 1995**

FDA's ENT Advisory Panel Meeting  
Presentation of Cochlear's Nucleus 22 Cochlear Implant  
PMA application- expansion of patient population  
Rockville, Maryland  
**April, 1995**

Second Symposium of Society for Acupuncture Research (SAR)  
Georgetown University Conference Center  
Government's perspectives on clinical trials for acupuncture  
Washington, D.C.  
**September 17, 1994**

**FDA's CHAIRMAN**

Reuse of Hemodialyzer,  
Rockville, Maryland  
**December 10, 1993  
May 1995**

**LECTURES, INTERVIEWS & ACTIVITIES After FDA:**

**FDA and Acupuncture**  
ABC News Interview  
Los Angeles, CA  
**Summer 1995**

**Dealing with Adverse Events**

1996 National Sales Meeting  
Johnson & Johnson Medical Inc.  
Dallas, Texas  
**April 1, 1996**

**Dialyzers Labeled for Reuse**

The Manufacturer's Responsibilities  
Fifth Annual Spring Clinical Nephrology Meeting  
National Kidney Foundation  
Anaheim, CA  
**April 27, 1996**

**Challenges with Infusion Therapy Complications**

Intravenous Nursing Society  
Charlotte, North Carolina  
**May 7, 1996**

**510(k) Tutorial**

Food Drug and Law Institute  
40th Annual Educational Conference  
Washington, D.C.  
**December 9, 1996**

**FDA Expert Panel Member**

Medical Devices: Device Labeling Requirements  
Center for Devices and Radiological Health  
Food and Drug Administration  
Rockville, MD  
**September 5, 1997**

**Science and Art of Designing Successful Medical Device**

**Clinical Trials for the FDA- A Workshop**  
Institute for International Research, Pharmaceutical Division  
Santa Monica, CA  
**September 22-24, 1997**

**What You May Need to Know about Medical Devices  
And FDA But Never Would Have Thought to Ask.**

22nd Annual Great Lakes Biomedical Conference

Engineering in Medicine and Biology Society

Milwaukee School of Engineering

Milwaukee, Wisconsin

**April 3, 1998**

**ABC News Interview with Ron Regan**

Medical Device Reporting for Surgical Trocar Injuries

WEWS ABC - Channel 5 News

Cleveland, Ohio

**May 17, 2001**

Interview in: *The Trouble with Trocars*

By Linda Carroll & Alfred Lubrano

Smart Money

**The Wall Street Journal Magazine of Personal Business**, Hearst Communications

New York, NY

**November 2001**

**FDA Inside and Out- Public Health Issues in Cervical Cancer Screening**

Global Vista Medical Foundation

Sponsored by President Medical technologies Co., LTD

Taipei, Taiwan, R.O.C.

**March 3, 2002**

**Inside the FDA**

Presentation to Kent County Medical Society

Grand Rapids, MI

**May 14, 2002**

**Clinical Trials**

**What physicians need to know about FDA.**

Medical Grand Rounds

St. Mary's Hospital

Grand Rapids, MI

**May 15, 2002**

Interview in ***The Risky World of Medical Implants***

A Three Part Series

Robert Cohen and J. Scott Orr

Star Ledger

Morris Edition, New Jersey

**August 11-13, 2002**

NBC's **Dateline** Interview with Lea Thompson

Special Investigations- **Do No Harm-Sulzer's Hip Recall**

NBC News Washington

Washington, D.C.

\*2004 Emmy Outstanding Investigative Reporting Business News Story

\*2004 Edward R. Morrow Television Investigative Reporting

**July 25, 2003**

Interview with Author Barbara Seaman

**History of FDA's Clearance of Bone Densitometers**, page 78

The Greatest Experiment Ever Performed on Women

Published by Hyperion, New York, New York

**Fall 2003**

Interview **Is This Any Way to Have a Baby? The Terrifying Truth About Fertility Drugs.**

Barbara Seaman and Joanna Perlman

OPRAH Magazine, beginning page 188

Published by Hearst Communications Inc., New York, New York

**February 2004**

Interview **Warning! The Medical "Miracles" That May Be Hazardous to Your Health.**

Alexis Jetter

Good Housekeeping Magazine, beginning page 138

Published by Hearst Communications Inc., New York, New York

**March 2004**

Interview **Investigation of FDA's Oversight of Mammography Facilities**

Producer Mary Schwager

Investigative News

WHDHTV-NBC

Boston, MA

**October 19, 2004**

**Bayer Stroke Trial Continues**

Tim Gurrister

Top of Utah

Salt Lake City, UT

**January 22, 2005**

**Drugs, Informed Consent and Monitoring to Ensure Safety of Women for Stem Cell Donation**

Open Letter of Suzanne Parisian, MD

Presented to California Legislature and Massachusetts Legislature

Released **February 2005**

**Open Letter Suzanne Parisian, MD**

Chapter 25- **Infertility and Assisted Reproduction**

Emerging Biotechnologies: Cloning

**Our Bodies Ourselves**

Boston Women's Health Book Collective, Inc.

Boston, MA

**March 2005**

**Interview Stem Cell Research & Egg Donation**

Martha Bebinger

WBUR NPR Radio

Boston, MA

**April 2, 2005**

**Interview in Exposed Nerve**

Craig Malisow

Houston Press

Houston, TX

**April 7, 2005**

**Public Statement-Regarding Two Pending PMAs**

On Behalf of ProChoice Alliance for Responsible Research (PROCARR)

General & Plastic Surgery Devices Panel

Center for Devices and Radiological Health

Food and Drug Administration

Gaithersburg, MD

**April 11, 2005**

**FDA's History of Silicone-Gel Filled Breast Implants**

Briefing of US House of Representatives and US Senate Staff  
Washington, DC

**April 25, 2005**

**Conference - Two Pending PMAs**

Presentation to FDA Commissioner Dr. L. Crawford  
Food and Drug Administration

Washington, DC

**April 26, 2005**

**Public Statement – Two Pending License Applications**

Health Canada Therapeutic Products Expert Review Panel  
Ottawa, Canada

**September 29, 2005**

**FDA & CLIA**

**Trends in Medical Diagnostic Commercialization**

Arizona Biotechnology Association

Phoenix, AZ

**February 7, 2006**

**ABC Interview Nightline**

**Fertility Myth**

Producer Mary C. Foster

**May 30, 2006**

**Interview FDA and IVF Donor Safety**

Penumbra Films

Documentary Name TBD

**March 17, 2007**

**Regulatory Affairs Professional Society (RAPS)**

Web-Based Class

Faculty

Medical Devices: Definition and Lifecycle

**January 2008**

**The Pathologist's Role in Preserving Implanted Cardiac Pacemakers  
And Defibrillators or "How Not to get Shocked!"**

American Academy of Forensic Sciences Annual Meeting

Washington DC

**February 22, 2008**

Interview **IVF**

Producer Jack Hafer

Boulevard Pictures

Documentary

**Lines That Divide The Great Stem Cell Debate**

**May 21, 2008**

KHPO NEWS FOX Network

Interview Kara Liu

FDA: Beware Tainted Weight Loss Drugs

**March 23, 2009**

**A New Washington- The Impact on the Bioscience Industry  
Trends at the FDA**

BIOZONA 2009

Arizona's Annual Bioscience Industry Conference

**April 7, 2009**

**Your Role with New Drugs/Medical Devices**

Wayne State University

Department of Biomedical Engineering & Wayne State Medical School

**June 24, 2009**

**How Did That Drug/Medical Device Ever Get to Market? Legal Aspects of Drug and  
Device Approval.**

Wayne State University Law School

**June 25, 2009**

**Consultation for FDA Issues**

Center for Arizona Policy

House Engrossed Senate Bill

Amending Title 36, Arizona Revised Statutes, By Adding Chapter 11; Relating to Human Eggs

Forty-ninth Legislature, Second Regular Session 2010

State of Arizona, Phoenix, AZ

**March 18, 2010**

## **VOLUNTARY STANDARDS COMMITTEE INVOLVEMENT**

Has been an active member of the following committees for  
**AMERICAN SOCIETY for TESTING MATERIALS (ASTM)**  
Medical and Surgical Material and Devices  
Occupational Health and Safety  
Search and Rescue  
Anesthetic and Respiratory Equipment  
Forensics  
Biotechnology

**AMERICAN ASSOCIATION FOR THE ADVANCEMENT  
OF MEDICAL INSTRUMENTATION (AAMI)**  
Renal Disease and Detoxification Committee

## **PUBLICATIONS:**

*Homoeotic Effect of the Tumorous-Head Mutant and Differential Effect of an Enhancer Gene in the Tumorous-Head Strain of Drosophila Melanogaster, Canadian J Genet. and Cytology, 1975; 17:423-432.*

*Latex Allergy and Anesthesiology.*  
*Anesthesia Patient Safety Foundation Newsletter*  
Spring, 1992.

*The Potential for Adverse Reactions Due to the Presence of Additives and Preservatives in Intravenous Solutions and Medications; Journal Vascular Access Devices, Winter 1996, Vol 1 (1): 5-14.*  
\*Sponsored by Johnson & Johnson Medical, Inc.

*Letter to the Editor, Midline Catheterization in Hospitalized Patients.*  
*Annals of Internal Medicine*, October 15, 1996; Vol 125, No 8: p 697.  
\*Sponsored by Johnson & Johnson Medical, Inc.

**FDA INSIDE and OUT,**  
S. Parisian, M.D.  
Publication May, 2001  
*Fast Horse Press, Inc.*

**DATE AND PLACE OF BIRTH:**  
September 20, 1952,  
Rapid City, Pennington County, South Dakota

**MARITAL STATUS:**

Married- August 26, 1977

**FAMILY:**

Son 02/09/1985

Daughter 09/12/1986

**MEDICAL LICENSURE:**

State of Virginia

State of Arizona

**EDUCATION:**

**6/1970-6/1974** Bachelors of Science

University of Central Florida

Orlando, Florida

**7/1974-6/1975** Masters of Science

University of Central Florida

Orlando, Florida

**7/1975-6/17/1978** Medical Doctorate

University of South Florida

Tampa, Florida

**TRAINING:**

**7/1/1978-6/30/1979** Flexible Internship

Greenville Hospital System

Greenville, South Carolina

**9/14/1981-6/30/1982** Pathology Resident

University of California, San Diego

San Diego, California

**7/1/1982-2/29/1984** Pathology Resident

University of Southern California

Los Angeles County Medical Center

Los Angeles, California

**1/4/1988-1/30/1990** Pathology Resident

Grand Rapids Area Medical Education Center

Grand Rapids, Michigan

**BOARD CERTIFICATION:**

Board Certified in Anatomic and Clinical Pathology, 1989, American Board of Pathology  
College of American Pathologists, Fellow (FCAP)  
American Society of Clinical Pathologists, Fellow (FASCP)

**SOCIETIES:**

American Medical Association  
Arizona Medical Association  
Arizona BioIndustry Association  
Maricopa County Medical Society  
American Advancement for Medical Instrumentation  
American Society for Testing Materials  
Regulatory Professionals Society  
Food and Drug Law Institute  
College of American Pathologists  
Food and Drug Alumni Association

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E-Mail: [info@mdassist.com](mailto:info@mdassist.com)

**WEBSITE:**

<http://www.mdassist.com>

7/7/14

## APPENDIX B

### LEGAL TESTIMONY HISTORY

**Suzanne Parisian, M.D.**

### COURT TESTIMONY

**January 2012-February 24, 2017**

- 10/20-21/15** Pamela Rheinfrank, Individually, and as Parent and Natural Guardian of M.D. v. Abbott Laboratories and Abbvie, Inc.  
Civil Action No.:1:13-CV-144  
In the United States District Court for Southern District of Ohio  
Western Division, OH
- 05/18/15** Deborah Barba & Thomas D. Barba v. Boston Scientific Corp,  
Superior Court of the State of Delaware In and For New Castle County  
C.A. No. N11C-08-050  
Wilmington, DE
- 02/3-4/15** Kevin Phillips v. C.R. Bard, Inc., et. al.  
3:12-cv-00344-RCJ-WGC  
United States District Court District of Nevada  
Reno, NV
- 11/12-13/14** Louise Taylor v. Johnson & Johnson, Inc., Janssen Pharmaceutica, Inc., et. al.  
Cause No. 2002-0389  
Circuit Court of Copiah County, Mississippi
- 8/13-14/14** Louise Taylor v. Johnson & Johnson, Inc., Janssen Pharmaceutica, Inc., et. al.  
Cause No. 2002-0389  
Circuit Court of Copiah County, Mississippi
- 05/08/14** In RE: Zometa/Aredia Litigation  
Jimmy Earp and Patricia Earp v. Novartis Pharmaceuticals Corp  
Case No. 5:2011cv00680  
North Carolina Eastern District Court, Western Division Office  
Raleigh, NC

- 04/25/14** In RE: Actos Related Cases No. 2011 L 010011  
Diane Whitlatch & Estate William Whitlatch No. 2012 L 006087  
v. Takeda Pharmaceuticals America, Inc.: et al.  
County Dept., Law Division  
In the Circuit Court of Cook County, Illinois  
Chicago, IL
- 03/26/14** In RE: Zometa/Aredia Litigation  
Ruth Dopson-Troutt v. Novartis Pharmaceuticals Corp  
Case No. 8:06-CV-1708-T-24-EAJ  
United States District Court Middle District, Tampa Division  
Tampa, FL
- 09/11/13** In RE: Zometa/Aredia Litigation  
Nancy Guenther & Donald Guenther v Novartis Pharmaceuticals Corp  
Case No.6: 08-cv-456-Orl-31DAB  
United States District Court Middle District of Florida, Orlando Division  
Orlando, FL
- 6/11-12/13** In RE: Zometa/Aredia Litigation  
Chris Hill v Novartis Pharmaceuticals Corp  
Case No.1: 06-CV-00939-JSR-SAB  
United States District Court Eastern District of California  
Fresno, CA
- 4/30/13** In RE: Zometa/Aredia Litigation  
Beverly Meng v. Novartis Pharmaceuticals Corporation  
Case No. 278 MT  
Superior Court of New Jersey  
Law Division: Middlesex County  
New Brunswick, NJ
- 4/19/13** In RE: Zometa/Aredia Litigation  
Keith Taylor v Novartis Pharmaceuticals Corp  
Case No: 06-61337-CIV-COHN/SELTZER  
United States District Court Southern District of Florida  
Ft. Lauderdale, FL
- 4/17/13** Fred Taylor and Josette Taylor v. Intuitive Surgical, Inc.

No. 09-2-03136-5  
Superior Court of the State of Washington in and for Kitsap County  
Port Orchard, WA

- 4/10,11/13** In RE: Zometa/Aredia Litigation  
Adrian Georges v. Novartis Pharmaceutical Corp.  
Case No. 2:06-cv-05207  
United States District Court Central District Court of California  
Los Angeles, CA
- 3/4/2013** In RE: Zometa/Aredia Litigation  
Charlotte Payne v. Novartis Pharmaceutical Corp.  
United States District Court Eastern District of Tennessee at Chattanooga  
Chattanooga, TN
- 2/13/13** In RE: Zometa/Aredia Litigation  
J. Hunter Chiles, III, et. al. v. Novartis Pharmaceutical Corp.  
Case No. 3:06-cv-96-J-25 JBT  
United States District Court Middle District of Florida  
Jacksonville Division, FL
- 1/24,28/13** In RE: Fosamax Product Liability Litigation  
Rhoda E. Scheinberg v. Merck & Co., Inc.  
Case No. 1:08-cv-04119-JFK  
United States District Court, Southern District of New York  
New York, NY
- 12/5-7/12** In RE: Prempro Products Litigation  
Lewis v. Wyeth et al.  
Case No.: 4:06-cv-01383-BRW  
United States District Court Eastern District of Arkansas Western Division  
Little Rock, AK
- 10/16, 18/12** In RE: Zometa/Aredia Litigation  
Barbara Davids v. Novartis Pharmaceutical Corp.  
Case No. CV-06-0431- ADS  
United States District Court Eastern District of New York  
Central Islip, NY
- 10/04/12** In RE: Zometa/Aredia Litigation

Irene Jenkins v. Novartis Pharmaceutical Corp.  
Case No. 3:11-CV-342  
Sandra Thorn  
Case No. 3:11-CV-373  
United States District Court Eastern District of Tennessee at Knoxville  
Knoxville, TN

**9/20/12** In RE: Zometa/Aredia Litigation  
V. Brown v. Novartis Pharmaceuticals, Corp.  
Case No. 7:08-CV-130-FL  
In the United States District Court for the Eastern District of North Carolina  
Southern Division  
New Bern, NC

**9/14/12** In RE: Zometa/Aredia Litigation  
V. Brown v. Novartis Pharmaceuticals, Corp.  
Case No. 7:08-CV-130-FL  
In the United States District Court for the Eastern District of North Carolina  
Southern Division  
New Bern, NC

**8/22-24/12** In RE: Prempro Products Litigation  
T. Okuda v. Wyeth et al.  
Case No: 1:04cv-00080  
United States District Court of Utah  
Salt Lake City, UT

**8/15-20/12** In RE: Prempro Products Litigation  
S. Welch v. Wyeth, et al.  
MDL No. 1507 No. 4:03CV01507  
Case No 4: 06CV00299-BRW  
United States District Court Eastern District of Arkansas Western Division  
Little Rock, AK

**6/21/12** In RE: Prempro Products Litigation  
Baldonado v. Wyeth, et. al.  
Case: 1:04-cv-04312  
United States District Court, Northern District of Illinois  
Chicago, IL

**6/19/12** Janelle Barnes v. Orthofix International NV

Case No. C11-402JCC  
United States District Court, Western District of Washington at Seattle  
Seattle, WA

- 5/30/12** In RE: Zometa/Aredia Litigation  
Zimmerman v. Novartis Pharmaceuticals, Corp.  
No. 08-cv-02089-RWT  
United States District Court of Maryland  
Baltimore, MD
- 03/23/12** In RE: Zometa/Aredia Litigation  
Christine Winter, et al. v. Novartis Pharmaceuticals, Corp.  
No. 06-4049-CV-C-MJW  
United States District Court for the Western District of Missouri, Central Division  
Jefferson City, MO
- 03/22, 26/12** In RE: Fosamax Product Liability Litigation  
Joanne Sessner v. Merck Sharp &Dohme Co., Inc.  
Docket No. ATL-L3394-11 MT  
Superior Court of New Jersey Law Division: Atlantic, City  
Atlantic City, NJ
- 03/12-14/12** In RE: Prempro Products Litigation  
J. Schutter v. Wyeth, et. al.  
Case No. 1:05-cv-0998  
United States District Court, N.D. Illinois, Eastern District  
Chicago, IL
- 02/14-16,  
21/12** In RE: Prempro Products Litigation  
S. Kammerer, et. al. v. Wyeth, et. al.  
Case 8:04CV196  
United States District Court for District of Nebraska  
Omaha, NE
- 01/24-5/12** In RE: Zometa/Aredia Litigation  
Sharon Brodie v. Novartis Pharmaceuticals Corporation  
United States District Court  
Case No. 4:10-CV-138 HEA  
Eastern District of Missouri, Eastern Division  
St. Louis, MO
- 01/13/12** In RE: Zometa/Aredia Litigation

Mahaney/Kyle v. Novartis Pharmaceuticals Corporation  
Case 1:06-cv-0035-TBR  
United States District Court, Western District of Kentucky  
Bowling Green, KY

**01/09/12** In RE: Avandia Drug Cases  
Janet Johnson v. SmithKline Beecham Corp, d/b/a GlaxoSmithKline, et al.  
Case No. INC072316  
Case No. JCCP No. 4578  
Superior Court of the State of California  
County of Los Angeles, CA

**DEPOSITION TESTIMONY**  
**January 2012- February 24, 2017**

**02/16/17** In RE: Yasmin and Yaz (Drospirenone) Marketing, Sales Practices and Products  
Liability Litigation  
3:09-md-02100-DRH-PMF  
Susan Galinis et el. v. Bayer Corporation et. al.  
MDL No. 2100  
United States District Court Southern District of Illinois  
Illinois

**12/8&9/16** In RE: XARELTO (Rivaroxaban) Products Litigation  
MDL No. 2592 Section L. Judge Eldon E. Fallon, Mag. Judge North  
United States District Court for the Eastern District of Louisiana  
State of Louisiana

**09/13/16** Kathy Moughler et al v. Abbott Laboratories and Abbvie Inc.  
Civil Action No. 2:14-cv-00081-WOB-CJS  
United States District Court for the Eastern District of Kentucky  
Northern Division at Covington, KY

**09/01/16** Doris Civale v Davol Inc., Bard Devices Inc., and CR Bard Inc.  
Docket N: L-3158-13  
Superior Court of New Jersey  
State of New Jersey

**07/07/16** Rhonda Orrick, as Next Friend of Dylan Enders, a minor, et al v SmithKline  
Beecham Corporation, d/b/a GlaxoSmithKline and GlaxoSmithKline, LLC  
Cause No. 1322-CC00079-01 Division 2

Missouri Circuit Court  
Twenty-Second Judicial Circuit  
St. Louis City, MO

- 06/28/16** D. Anders, et al. v Medtronic, Inc., Medtronic Sofamor Danek, USA, Inc, and  
DOES 1-100  
Case No. 1322-CC10219-02, Division 5  
In the Circuit Court of the City of St. Louis  
State of Missouri
- 06/14/16** Ernesteen Jones v Novartis Pharmaceuticals Corp  
No.: CV-13-00624-VEH  
United States District Court Northern District of Alabama  
Southern Division  
Birmingham, AL
- 06/07/16** Marvin Copley, Tiffany Copley, Parents & Aedan Copley, deceased v Bayer  
Healthcare Pharmaceuticals, Inc.  
Case No: 2014-cv-902242  
In the Circuit Court of Mobile County, Alabama  
Birmingham, AL
- 05/16/16** Teddy James Washington v Wright Medical Technology, Inc.  
Case No. BC576878  
Superior Court of the State of California  
County of Los Angeles  
Los Angeles, CA
- 04/08/16** In RE: Kugel Mesh Hernia Patch Products Litigation  
MDL Docket No. 07-1842-ML  
Norma Olmo et al v Davol Inc., C.R Bard, et al  
Case No. No. 1:13-cv-03820-ML-LDA  
United States District Court District of Rhode Island  
Providence, RI
- 03/08/16** In RE: Ethicon, Inc. Pelvic Repair System Products Liability Litigation  
Master File No. 2:12-MD-02327  
United States District Court Southern District of West Virginia at Charleston  
Charleston, WV
- 10/05/15** B. Tucker v Wright Medical Technology, Inc., et al  
Case No. BC575110

Superior Court of the State of California  
County of Los Angeles  
Los Angeles, CA

- 09/14/15** In RE: AMS Pelvic Mesh Products Liability Litigation  
Marylyn Carter v AMS  
Master Docket C.A. No. 11C-07-212 MMJ  
C.A. No. N10C-05-209-MMJ  
In the Superior Court of the State of Delaware in and For New Castle County,  
Wilmington, DE
- 09/03/15** In RE: Mirena® IUD Products Litigation  
Superior Court of New Jersey Law Division: Bergen County Case No. 297  
Master Docket No.: BER-L-4098-13  
United States District Court Southern District of New York
- 06/26/15** Anne Tolentino v. Bayer Corporation, et al.  
No. 02596  
In the Court of Common Pleas  
Philadelphia County, PA
- 06/18/15** Denise Kilgore v. Mark Curry D.O. & American Medical Systems, Inc.  
Case No.:14CV01312 Division: 3  
In the District Court of Johnson County, Kansas Civil Court Department  
Kansas City, KS
- 06/11/15** In RE: YAZ/Yasmin/Ocella (Drospirenone) Marketing Sales Practices and  
Products liability Litigation  
3:09-md-2100-DRH-PMF  
MDL No. 2100  
United States District Court, Southern District of Illinois  
Illinois
- 05/20/15** Donna Cox v John M. Moore, MD, Pliva  
Cause N. 1316-CV26473 Division 2  
Circuit Court of Jackson County, Missouri at Independence  
Missouri
- 05/05/15** George Gaston v C.R. Bard, Inc. et al  
Civil Action No. 2:13-cv-00236-KS-MTP  
United States District Court for the Southern District of Mississippi  
Eastern Division

Jackson, MS  
Henry Kilver & Judy Kilver v C.R. Bard, Inc. et al  
Case No. 1:13-cv-01219-MMM-JAG  
United States District Court Central District of Illinois  
Peoria, IL

- 04/23/15** Eleanor Fulgenzi v Pliva, Wyeth et al  
Case No. 5:09-cv-01767  
United States District Court for the Northern District of Ohio, Eastern Division  
Akron, OH
- 02/12/15** Sandra Garcia v. Rodolfo Walss, M.D. Johnson & Johnson, Inc. and Ethicon, Inc.  
Cause No. 2013-DCL-3511-D  
In the District Court 103<sup>rd</sup> Judicial District  
Cameron County, TX
- 01/08/15** In RE: Wright Medical Technology, Inc. Conserve Hip Implant Products  
Litigation  
Robyn Christiansen & Gene Christiansen v. Wright Medical Technology, Inc.  
MDL No. 2329  
In United States District Court, Northern District of Georgia, Atlanta Division  
Atlanta, GA
- 12/18/14** George Leus v C. R. Bard, Inc., Bard Peripheral Vascular, Inc.  
Case No. 4:13-cv-00585-GAF  
United States District Court for the Western District of Missouri  
Western District, MO
- 10/07/14** Pamela Rheinfrank, Individually, and as Parent and Natural Guardian of M.D. v.  
Abbott Laboratories and Abbvie, Inc.  
Civil Action No.:1:13-CV-144  
In the United States District Court for Southern District of Ohio  
Western Division, OH
- 09/25/14** Mary Giordano on Behalf of Estate of Jacqueline Keith vs C. R. Bard, Inc., Bard  
Peripheral Vascular, Inc.  
Case No. 37-2011-00069363-CU-PO-EC  
Superior Court of California, County of San Diego, East County Regional Center  
San Diego, CA

**07/09/14** Janis E. Thompson v. American Medical Systems, Inc.  
Case No. 12CV1767 Division 2 Chapter 60  
In the District Court of Wyandotte County, Kansas  
Civil Court Department  
Kansas City, KS

**06/13/14** Keven Phillips v. C.R. Bard, INC, Bard Peripheral Vascular, INC.  
Case No. 3:12-cv-00344-RCJ-WGC  
United States District Court District of Nevada  
Las Vegas, NV

**3/12-13/14** Diane Albright v. Boston Scientific Corp, et.al.  
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Maria Cardenas v. Boston Scientific Corp, et.al.  
Civil Action No. MICV2012-02912  
Ronda & Tony Orozco v. Boston Scientific Corp, et.al.  
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Julia Wilson v. Boston Scientific Corp, et.al.  
Civil Action No. MICV2012-02626  
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**2/18/14** Melanie Martinez v American Medical Systems., et al  
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**12/19/13** In RE: Zometa/Aredia Litigation  
Gary Stevens v. Novartis Pharmaceutical Corporation  
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**11/05/13** In RE: Actos Related Cases No. 2011 L 010011  
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- 10/04/13** In RE: American Medical Systems, Inc. Products Liability Litigation  
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Debbie Jilovec, et. al. 2:12-CV-05561  
Joann Serrano, 2:12-CV-3719  
Mary Weiler, et. al. 2:12-CV-05836  
In the United States District Court for the Southern District of West Virginia  
Charleston Division, WV
- 08/06/13** Louise Taylor v. Johnson & Johnson, Inc., Janssen Pharmaceutica, Inc., et. al.  
Cause No. 2002-0389  
Circuit Court of Copiah County, Mississippi
- 08/29/13** Olivia Whitaker Duncan & Evan Duncan v. Breg, Inc. et al.  
Case No. 37-2011-00059708-CU-PL-NC  
San Diego County Superior Court  
Superior Court of the State of California  
County of Orange, CA
- 03/19/13** In RE: NuvaRing Products Liability Litigation  
Case 4:08-MDL-1964-RWS  
United States District Court Eastern District of Missouri  
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- 01/14/13**  
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Inc.  
No. 09-2-03136-5  
Superior Court of the State of Washington in and for Kitsap County  
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- 12/13/12** Veronica Dore et. al. v. Novartis Pharmaceuticals  
Civil Action No.: 2:06-cv-02271 (ES-CLW)  
United States District Court, District of New Jersey  
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- 11/28/12** Janice Childers v. Cynosure, Inc.  
Civil Action No. 09-CI-00365  
Commonwealth of Kentucky

Pike Circuit Court, Second Division, KY

- 10/29/12** In RE: Fosamax Products Liability Litigation  
Rhoda Scheinberg v. Merck & Co, Inc.  
Case N. 1:08-CV-4119-JFK  
United States District Court For the Southern District of New York  
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- 10/23/12** Kris Prather v. Abbott Laboratories, et al.  
Case No. 3:09-CV-573-R  
United States District Court Western District of Kentucky Louisville Division  
Louisville, KY
- 7/2/12** Aaron Massey and Tracey Massey, individually and as natural guardians of  
Myles Massey, a minor v. H&P Industries, Inc et al.  
No. 09-2-45506-6  
In the Superior Court of the State of Washington  
In and for the County of King  
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- 05/23/12** Corissa Allison et. al. v. Woo Yong Medical, et al. Case No 5:08-CV-00549  
Sarah Atwell vs. WYM Case No. 5:08-CV-00346-D  
Lindy Patterson v WYM Case No. 5-09-CV-00308  
United States District of North Carolina, Western District  
Katherine M. Baker v WYM Case No. 0:09-cv-02898-ADM-RLE  
Mary J. Block v WYM Case No.09-cv-1332-JRT-JJK  
United States District Court, District of Minnesota
- 05/15/12** Ronna Dalton, et al. v. Animas Corporation, et al.  
Civil Action No. 3:09-CV-354-H  
United States District Court, Western District of Kentucky at Louisville  
Louisville, KY
- 03/29/12** Francisco Colon Jimenez et. al. v. Advanced Medical Optics, Inc et. al.  
Case No. 09-2172 (BJM)  
United States District Court, District of Puerto Rico  
San Juan, PR
- 03/08/12** Janelle Barnes v. Breg, Inc.  
No. 11-00402 JCC  
United States District Court, Western District of Washington at Seattle  
Seattle, WA

# **EXHIBIT B**

MD ASSIST, INC

C.R. BARD, INC.

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SUPPLEMENTAL EXPERT REPORT

S. PARISIAN, M.D.

April 7, 2017

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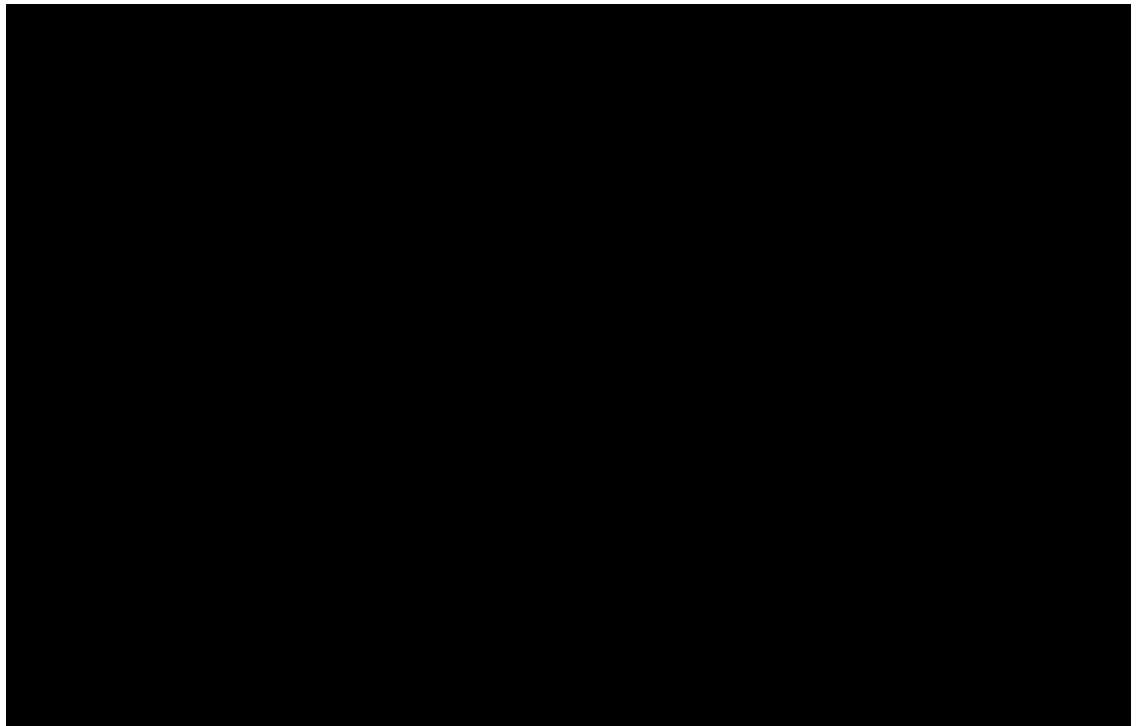
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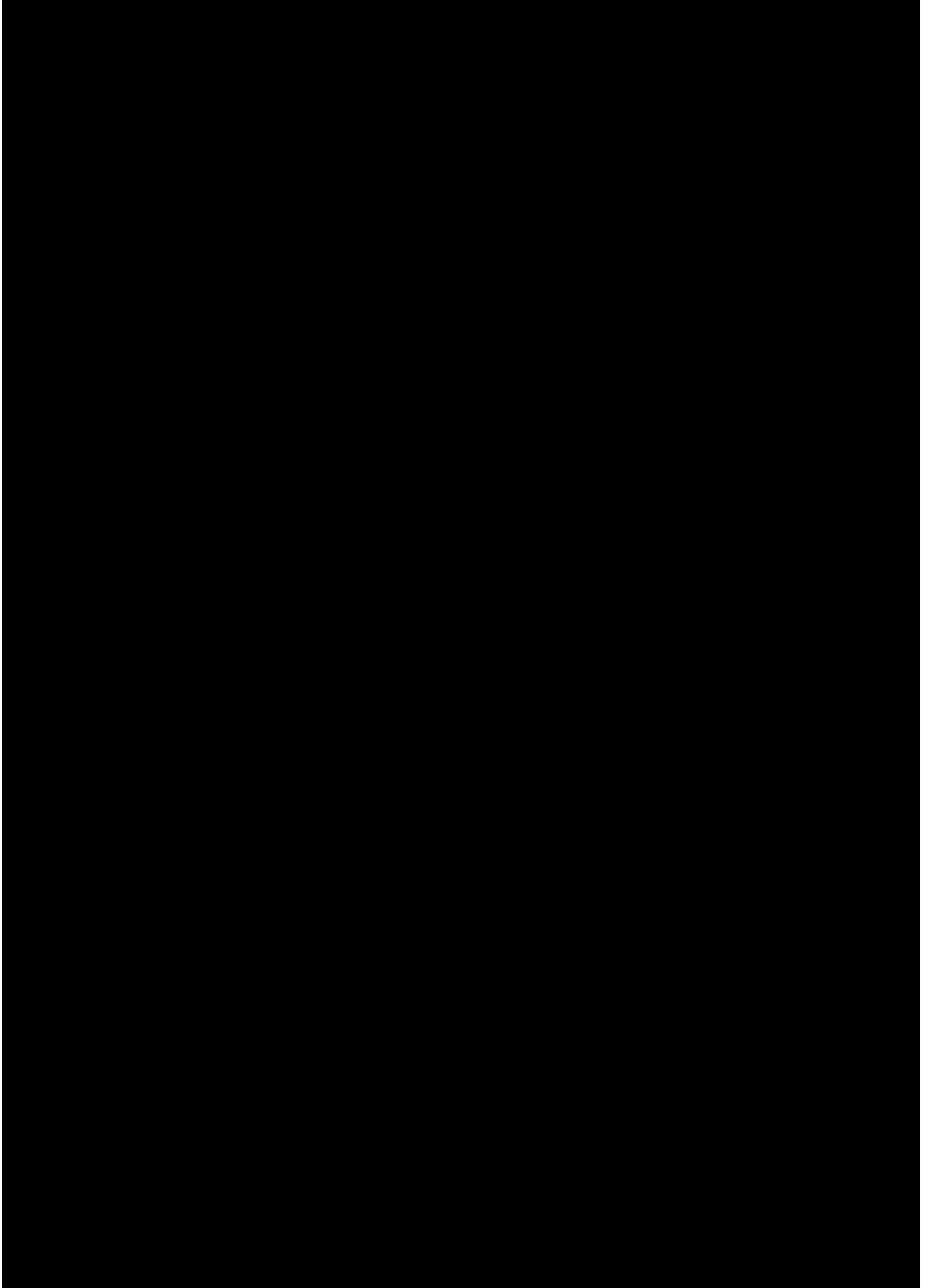
**SUPPLEMENTAL EXPERT REPORT OF  
SUZANNE PARISIAN, M.D.**

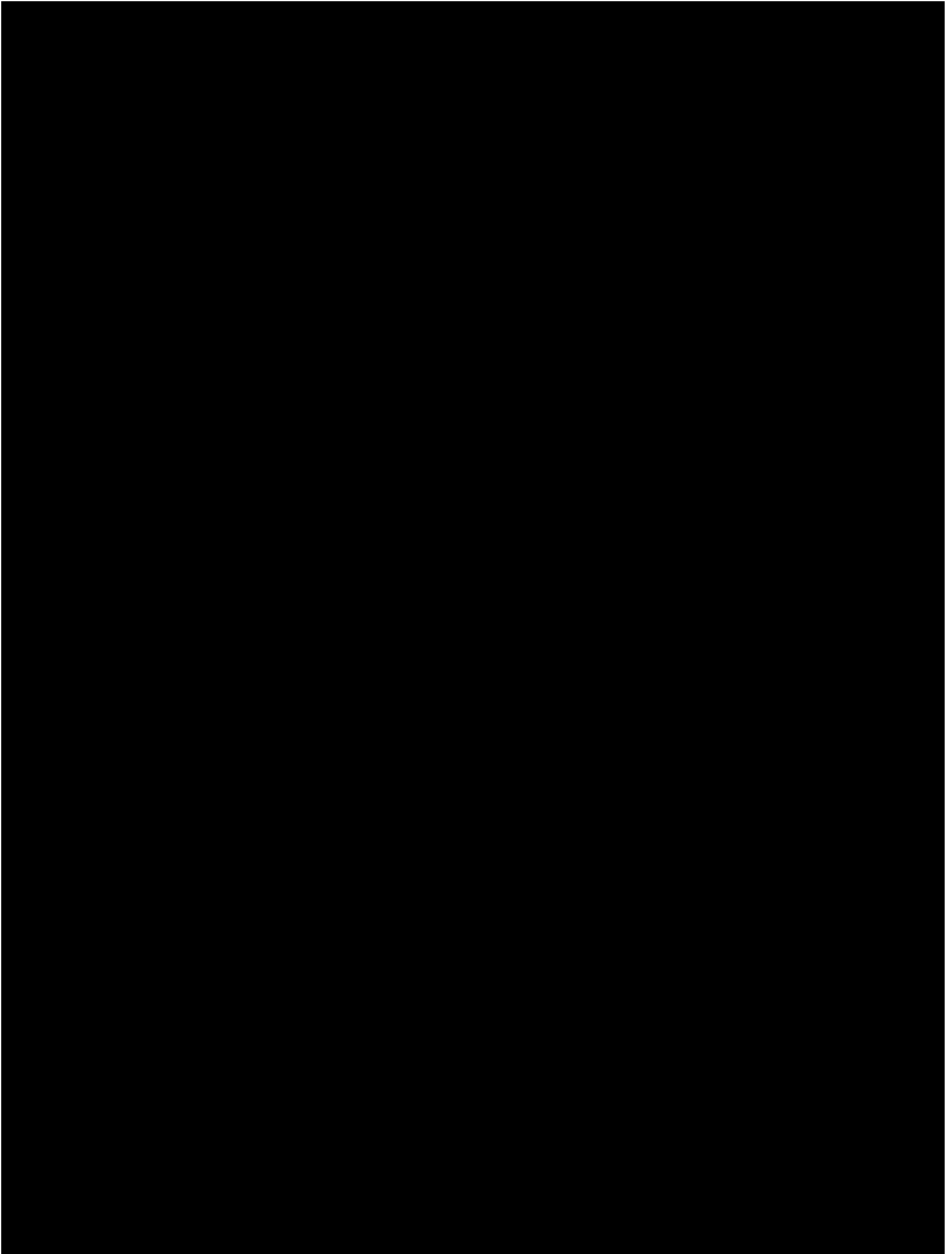
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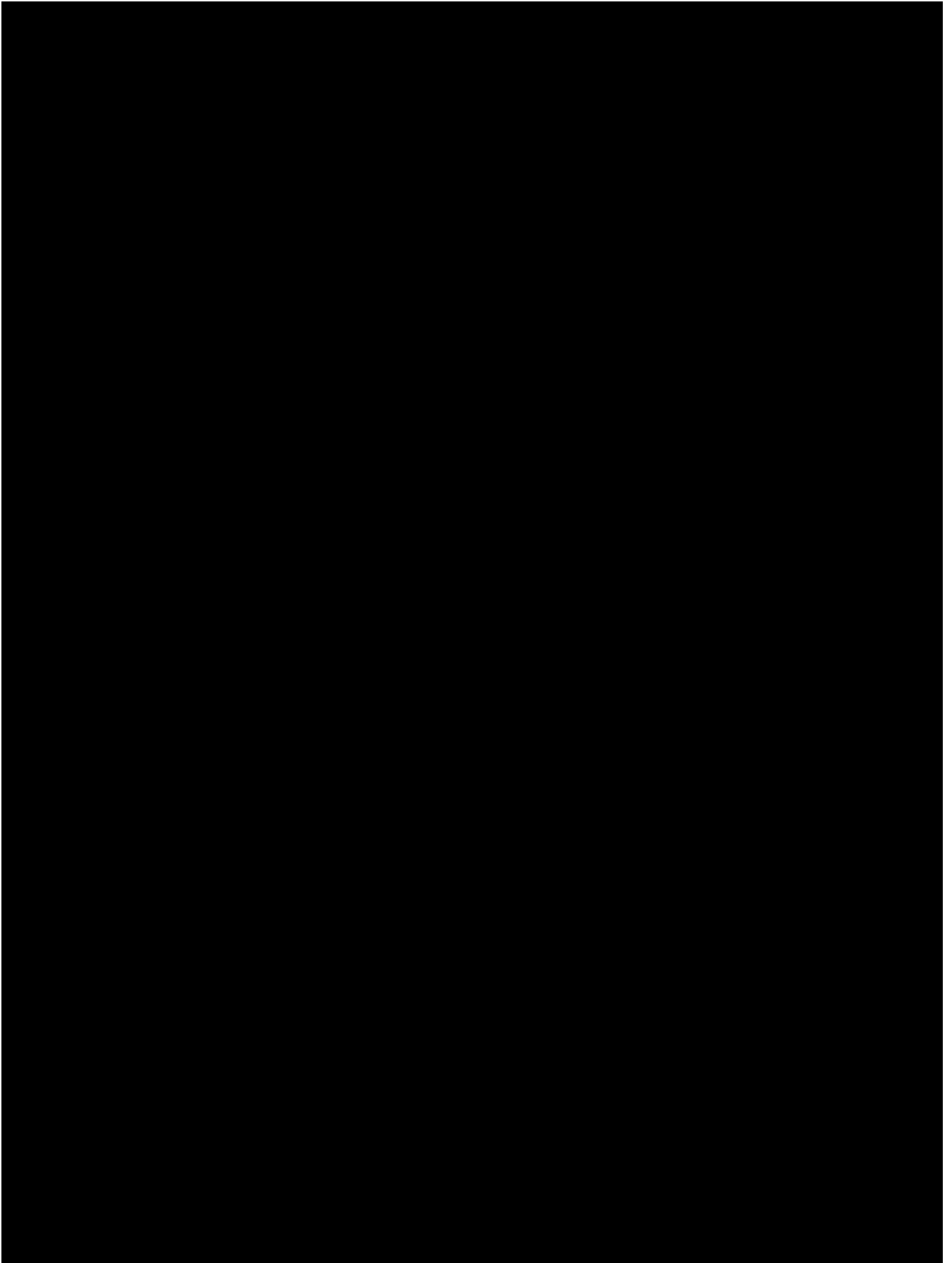
1. The following is written as an addendum to my prior Expert Report dated March 3, 2017. I have included additional information reviewed and considered regarding Bard's design and marketing of the later members of the RNF platform of devices sold as Meridian and Denali IVC Filters. I have attached a summary of six of my seven prior OPINIONS from my March Expert Report. The additional information for these two later Bard RNF IVC filters supplements and continues to support the prior opinions. For ease of reference I have listed the paragraphs in the March 2017 Expert Report supporting the OPINION as well as the relevant applicable regulations. The new information on Meridian and Denali does not change the prior opinions but I see them as additive, helping to complete the RNF regulatory history. I will attempt to briefly describe the new information reviewed and considered for Meridian and Denali IVC filters and place them in the framework of OPINIONS 1-6. I have not discussed OPINION #7, the Recovery Cone opinion, since there is no new information with Meridian and Denali that appears applicable to that OPINION.
2. My Curriculum Vitae is unchanged and attached for convenience as APPENDIX A. I have included the most current 5 years of deposition and court testimony, attached as APPENDIX B. I continue to receive \$400/hr. for study and \$600/hr. for deposition and trial testimony.
3. In the same format as the March 3, 2017 Expert Report, I have reviewed and relied upon the following supplemental Bard documents for development and commercialization of Meridian and Denali IVCs:

I. MERIDIAN DOCUMENTS:





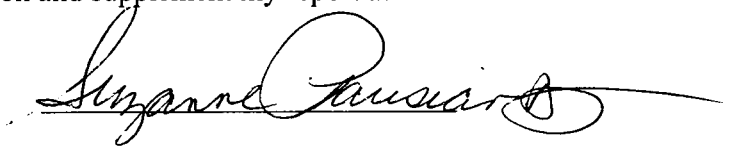






- Rebecca Betensky, Ph.D., Expert Report March 3, 2017

4. My opinions are all made to a reasonable degree of medical and regulatory certainty.
5. I reserve the right to amend my opinion and supplement my report at a later date.



Suzanne Parisian, M.D.  
April 7, 2017

**I. PRE-MARKET ACTIVITIES**

**OPINION #1: Bard’s premarket actions with design and development of the RNF as a permanent IVC filter were inadequate.**

[Refer to supporting bases in March 3, 2017, Dr. Parisian Expert Report: “Brief Overview of FDA’s and Medical Device Manufacturer Roles” ¶¶17-76 and OPINION #1 ¶¶ 77-210]

*Applicable Regulations:* 21 CFR § 807; 21 CFR § 860; 21 CFR § 820; 21 CFR § 806; 21 CFR § 801.109; 21 USC § 331(a) (b); 21 USC § 352(a)(f)(1)(2),(t); 21 USC § 321(n); 21 USC § 351

**OPINION #2: Bard obtained FDA’s Clearance to market the RNF as both a “Permanent & Retrievable” Filter yet, failed to provide physicians and patients with adequate updated ‘Instructions For Use’ (IFU) And ‘Warnings of Risks’.**

[Refer to March 3, 2017, Dr. Parisian Expert Report OPINION #2 ¶¶ 211-346)]

*Applicable Regulations:* 21 CFR § 807; 21 CFR § 801.109; 21 USC § 331(a)(b); 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n)

**OPINION #4: Bard developed its “Next Generation” of filters based on piecemeal reactive modifications to its flawed original RNF filter platform rather than use quality science and medical device design principles.**

[Refer to March 3, 2017, Dr. Parisian Expert Report OPINION #4 ¶¶ 457-651]

*Applicable Regulations:* 21 CFR § 820.198; 21 CFR § 820.30; 21 CFR § 820.100; 21 CFR § 820.75; 21 CFR § 820.250; 21 USC § 352(a)(f)(1)(2)

**A. THE MERIDIAN IVC FILTER: A “NEXT GENERATION” RNF FILTER WITH “CAUDAL ANCHORS”**

- 1. Bard sought to address physician’s concerns about the risk of caudal migration when it redesigned the RNF for marketing reasons not patient safety and sought to avoid conducting a clinical trial as part of FDA clearance of the Meridian filter.**

<sup>1</sup> BPVE-01-00786415

[REDACTED]

2. [REDACTED]

3. [REDACTED]

4. [REDACTED]

a. [REDACTED]

5. [REDACTED]

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<sup>2</sup> BPVE-01-00786415

<sup>3</sup> BPVE-01-00786415

6.

[REDACTED]

7.

[REDACTED]

8.

[REDACTED]

[REDACTED]

9.

[REDACTED]

---

<sup>4</sup> BPV-17-01-00149523

[REDACTED]

10. [REDACTED]

**c. Bard's fatigue testing did not describe the fractured arm anchor weld.**

11. [REDACTED]

12. [REDACTED]

---

<sup>5</sup> BPV-17-01-00149523

<sup>6</sup> ASTM F2129-06 Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices. This standard is intended to be used on a device in its final and finished form, as it would be implanted in a patient. It is assumed that reference methods have already been used for screening the material. It is intended to be used on metals that have a high resistance to corrosion. (www.ASTM.org); 372-375\_BPVE-01-00818477

<sup>7</sup>Guidance for Industry and FDA Reviewers/Staff FDA Guidance for Cardiovascular Intravascular Filter 510(k) Submissions November 26, 1999 [hereinafter "1999 Guidance"]

<sup>8</sup> BPVEFILTER-02-00023338

13.

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<sup>9</sup> 1999 Guidance

<sup>10</sup> 1999 Guidance

<sup>11</sup> **ASTM E739-91(98)** “Standard Practice for Statistical Analysis of Linear of Linearized Stress-life (S-N) and Strain-Life ([Epsilon]-N) Fatigue Data. This is a practice that pertains only to S-N and e-N relationships that may reasonably be approximated by a straight-line relationship for a specific interval of stress or strain. ASTM has:” because the actual fatigue life distribution is unknown, it is not recommended that (a) the S-N or e-N be extrapolated outside the interval of testing, or (b) fatigue life at a specific stress or strain amplitude be estimated below approximately the fifth percentile (P[similar] 0.05). As alternative fatigue models and statistical analysis are continually being developed, later revisions of this practice may subsequently present analyses that permit more complete interpretation of S-N and e-N data. **ASTM E468-11** Practice for Presentation of Constant Amplitude Fatigue Test Results for metallic materials was developed to communicate information of data derived from constant-force amplitude axial, bending, or torsion fatigue tests of metal materials at room temperature, **ASTM E606/E606M-** Test method for Strain-Controlled Fatigue Testing.

[REDACTED]

14. [REDACTED]

15. [REDACTED]

16. [REDACTED]

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<sup>12</sup> BPVEFILTER-02-00023338

<sup>13</sup> See March 3, 2017, Expert Report ¶¶ 485-486

<sup>14</sup> The RNF did not have ‘caval compression testing’ for K022236

17.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

18.

[REDACTED]

19.

[REDACTED]

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[REDACTED]

for corrosion after fatigue testing was still visual using 40X magnification. A 5lb proof load was placed on each individual arm, wrist, shoulder, leg anchor following evaluation of all samples for evidence of fracture or corrosion (at 40x). All appendages (144 arms and legs) and all shoulder anchors (36) held the 5lb proof load following the completion of 4,000,000 cycles under test conditions.

20. Bard identified that the weld characterization of one wrist anchor did not support the 5lb load (1/36). Before loading, the wrist anchor had been noted to be intact. The anchor separated cleanly from the filter wire arm. The weld was found to be within specification, but there had been minimal weld penetration on the wire surface. The wire fractured at weld surface. At the time of testing the welding process had not been validated. Since there were no fractures produced at 4 Million cycles, and no areas of visible corrosion, the data presented for the diaphragmatic flat plate in vitro fatigue testing was said to demonstrate the long-term in vivo safety of the filter for up to 10 years. The recommendation at Bard was that the laser welding process for the anchors be validated and process controls further explored.<sup>17</sup>
21. Bard compared the Meridian to the historical data in a 1994 medical article for Boston Scientific's Stainless Steel Greenfield Filter (SSGF)<sup>18</sup> which Bard called the "gold standard" for IVC filter performance. This 1994 data published for SSGF showed "acceptable fatigue resistance when the filter was tested simulating an IVC deflections from 2.5cm to 1.0cm (25mm to 10mm) for up to 10 million cycles with 1 out of 10 filters fracturing (10%). The load chosen was to mimic maximal physiological changes that could occur in the human vena cava such as coughing."
22. In 2010, Bard indicated it had used the same method for testing the Denali IVC Filter, however, Bard did not provide comparator information for Denali to Meridian or to SNF. Bard's duration of the testing, unlike the SSGF was less than half the cycles, approximately 4 million cycles (not the 80 million cycles in the original testing design) <sup>19</sup> which Bard indicated was to be equivalent to 10 years of exposing the filter to diaphragmatic movements in a coughing patient. Chronic cough represented the worst-case scenario for Bard (coughing at a frequency of 43 coughs per hour, which equals 3.8 million coughs over a 10-year period, rounded to 4 million). So, Bard's simulation fatigue testing specification was initially intended to simulate 10 years implanted in a coughing patient (per TM1141700) rather than breathing and 80 Million cycles.<sup>20</sup>
23. Weld strength identified in the Diaphragmatic Fatigue Testing was examined after fatigue testing according to Bard was based on FDA's 1999 Guidance. The FDA's Guidance 1999, pre-clinical testing should be able to demonstrate "*sufficient fatigue resistance of the filter design.*" Based on the 510(k) clearance the Meridian fatigue resistance should be substantially equivalent to the SNF:

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<sup>17</sup> BPVEFILTER-01-01780607

<sup>18</sup> Bjarnason. *Investigative Radiology* (1994)

<sup>19</sup> TP-10-06-02 DV&V Resp Plate Fatigue & Corrosion Exam BPVEFILTER-02-00023338

<sup>20</sup> TP-10-06-02 DV&V Resp Plate Fatigue & Corrosion Exam BPVEFILTER-02-00023338

#### 4. Filter Fracture

*The filter's response to worst-case scenario respiratory and diaphragmatic movements in the vena cava under simulated respiratory cycles should demonstrate sufficient fatigue resistance of the filter design. In addition, there should be an examination of corrosion resistance and weld strength following cycling.*<sup>21</sup>

24. Not referenced by Bard, the 1999 Guidance placed the obligation of adequate testing to develop the Meridian on Bard, as well as the obligation to be familiar with the known history of its RNF family of filters when compared to the performance of the permanent SNF. *See* 21 CFR § 820.30; 21 CFR § 820.20; 21 CFR § 820.100; 21 CFR § 820.198; 21 CFR § 803; 21 USC § 331(a)(b); 21 USC § 351; 21 USC § 321(n); 21 USC § 352(a)(f)(1)(2),(t).

*The necessary array of tests for a particular filter will depend, in part, on the specific design. Therefore, this document may not reflect the complete battery of pre-clinical testing necessary to qualify all filters/designs...The degree to which a proposed device is similar to a currently marketed filter will indicate the level of testing necessary, i.e., whether the design characteristics can be assessed via in vitro bench testing, in vivo animal testing, clinical testing or some combination of all three.*<sup>22</sup>

25. 21 CFR § 820.30 addressed a sponsor's duty to develop adequate design controls based on both design inputs and outputs. The testing of the Meridian should have been compared to Bard's SNF, a permanent implant predicate to ensure substantially equivalent performance. Bard wrote its unsupported statements about FDA's requiring 10-year testing:

*Per the FDA Guidance Document-Cardiovascular Intravascular Filter 510(k) Submissions, the filter durability must be proven safe in vivo for up to ten (10) years of implantation life. Accelerated in vitro-fatigue testing is conducted in order to demonstrate this is a reasonable amount of time.*

*Previous testing of the Eclipse filter utilizing the same deflection parameters and demonstrated that the Eclipse filter was safe up to ten (10) years of implantation.*<sup>23</sup>

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<sup>21</sup> BPV-17-01-00149523

<sup>22</sup> November 26, 1999 FDA Guidance

<sup>23</sup> BPV-17-01-00149523

**d. Bard's comparative tilt testing did not adhere to Bard's protocol and still demonstrated poor performance of Meridian compared to Eclipse.**

26. The Meridian Design History File, Project #8120 TD-01964 July 18, 2011, from Brian Boyle has a "Bench Top Tilt Testing of Competitive Filters."<sup>24</sup> Testing was conducted on the Meridian, Eclipse, Celect, Tulip, and Option Filters. The Celect and Tulip were used for competitive benchmarking since the Cook filters represented the significant competition to Bard for the "optional filter" market. It is interesting to note that the Eclipse/Meridian (48.0) have the shortest filter heights of the optional implants examined.
27. Bard had 37% of market, Cordis 10%, Angiotech 9% and Cook Inc 44%. "Figure 3: Tilt in degrees VS compression cycle for competitive filters (lower tilt indicates better performance)" The graphic results showed that Eclipse actually had lower tilt per valsava (#) cycles than the new Meridian.<sup>25</sup> Bard's 510(k) did not inform the FDA that the Bench-top Tilt Testing of Competitive Filter showed less potential tilt over time for Eclipse than Meridian.

**e. Bard's comparative caudal migration testing to OptEase was significantly flawed.**

28. TP 10-08-09 was DV&V Caudal Migration Testing of Meridian and OptEase (Cordis) Filters.<sup>26</sup> The OptEase is a retrievable filter up to 14-days post implantation. Clinical trials with the OptEase have indicated that the filter is resistant to caudal migration. Bard's testing for Caudal Migration of Meridian and OptEase Filters TR-10-08-06, Appendix A August 19, 2010 provided the original datasheets for the testing. Testing was on June 28, 2010 and final sign off August 30, 2010. As not described in the TR-10-08-09 the OptEase IVCF test filters in Bard's 28mm simulation tube are commercial devices and for the 15 samples recorded, 7 OptEase filters are listed as "replaced" with maximum force values measured as: [62.74, 85.66, 84.85, 98.0, 113.6, 114.18 and 118.37]; another specimen with maximum force [118.14] called "not applicable" (N/A), with the filter listed as "tilted." The remaining 7 OptEase filters with maximum pressure ranging from [103.52-189.03] but are listed as "Rotated" with the "filter tilted, engaged more on one side." There is no OptEase filter that does not have a notation about rotation and tilt raising concerns about the ability of Bard to insert the OptEase filter correctly in the 28mm simulation tube to obtain a valid caudal migration resistance reading. It would not be anticipated that OptEase filters implanted in the 28mm tube that is both rotated and tilting (suboptimal placement) will provide a valid measurement of its effectiveness for resisting caudal migration.<sup>27</sup>
29. Based on the information in Appendix A-Original Datasheets, the testing of the Meridian versus the OptEase, appears skewed in favor of Meridian and, despite its later use by BPV

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<sup>24</sup> BPV-17-01-00149815

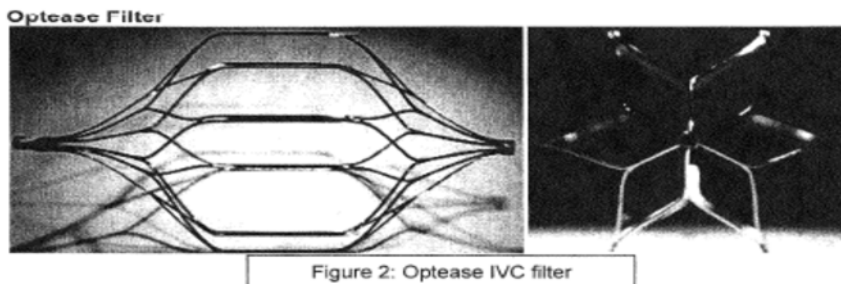
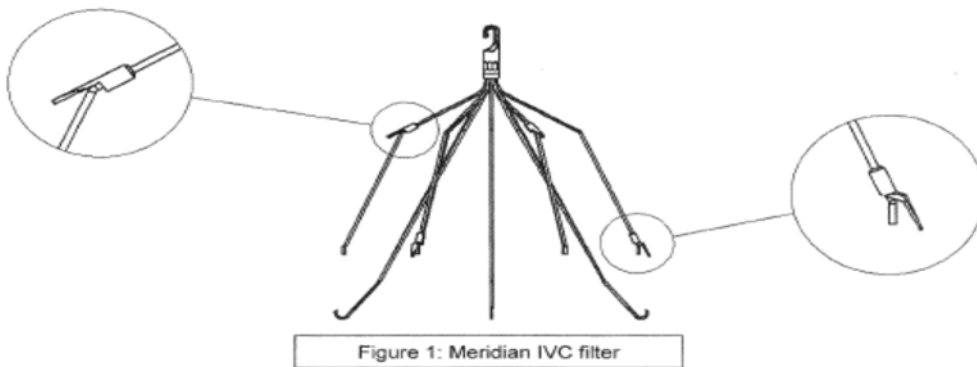
<sup>25</sup> BPV-17-01-00149815

<sup>26</sup> BPVE-01-02015283

<sup>27</sup> BPVE-01-02015283

for Marketing, does not appear to have been done in a manner to produce valid or meaningful scientific evidence.

30. All the Meridian samples came from one “Lot ESM-10-06-072” of Meridian Jugular Delivery System MD800J, sterilized twice by ETO. The OptEase filters came from seven commercial lots. The calibration of the Instron was June 28, 2011. The OptEase is intended to be placed in the IVC without tilting, is called self-centering and has six struts with fixation barbs present at the cranial end of the struts. It is designed for clot capture, and is made of laser cut from Nitinol. It is recommended to be removed from the patient at 14 days.



The Cordis OPTease® Vena Cava Filter (Filter) is designed for the prevention of recurrent pulmonary embolism via placement in the inferior vena cava (IVC). The self-centering OPTease Filter is laser cut from nickel titanium alloy (Nitinol) tubing. The proximal and distal baskets of the OPTease Filter, which consist of struts in a six diamond shape configuration, are designed for optimal clot capture. The baskets are connected by six straight struts. A single row of fixation barbs is present at the cranial end of the struts. These barbs, intended for

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31. BPV's Table 10 makes no indication that the 15 OptEase samples tested were all titled and rotated in the 28mm simulation tube. BPV also does not indicate the frequent association of 'wrist and shoulder anchor' perforation of the simulation tube. By the data on this table, Meridian range was [119.0-280.02 gf] and OptEase [62.7-196.2gf] There is not a discussion of the cause of the two low outlier values for Meridian that were dropped.

<sup>28</sup> BPVE-01-02015283

**f. Bard's Meridian vs. Eclipse caudal migration testing showed increased risk of Meridian anchor perforation.**

32. The same simulation study was done using Bard's IVC filters, both Eclipse and Meridian for maximum resistance to caudal migration.<sup>29</sup> This testing was performed on June 28, 2010, with sign off on August 20, 2010. There were 60 Bard filters, 30 were Eclipse and 30 were Meridian. The Eclipse filters are identified as "Reused" filters with maximum pressure ranging from [5.27 - 46.21 gf]-with almost no evidence of resistance to caudal migration. For the 30 Meridian Filter samples, 28 are listed as associated with some form of "wrist anchor perforation" and include both "replaced" and "reused" Meridian filters, with the maximum force for Meridian ranging from [22.07 -248.42gf]. The low value of 22.07 is associated with a 'rotational and reused' Meridian filters (B55), and is the only Meridian not recorded with wrist anchor perforation. A second Meridian filter B59-2 had a value of 33.07gf and is listed as Rotated for P14 and Reused with the 'sample replaced, original sample damaged'; Meridian specimen B60 had a maximum resistance of 168.36 gf and was listed as "replaced for P15" and "Reused" with 2 wrist anchors perforation, 1 shoulder anchor perforation, and the filter tilted. Specimen B58, with the highest maximum resistance of 248.42 gf was "Replaced for P13" and Reused, with 3 wrist anchors perforating; B56 had a maximum pressure of 205.56 gf and the notation replaced for P11, reused and with 3 wrist anchor perforation.<sup>30</sup> It appears that a Meridian wrist or shoulder anchor perforation (of the sausage casing lining the 28-mm simulation tube) can produce higher caudal migration resistance. However, the frequent perforation of the Meridian filter in the 28mm simulation tube raises a potential safety for a patient associated with the introduction of the wrist and shoulder anchors not seen with the Eclipse.

**10.0 RESULTS**

Table 4: Caudal Migration Test Results													
TM Number/ Description	Design Attribute	PPS 8120J Characteristic Level	Acceptance Criteria	Filter	Qty	Confidence / Reliability level	P- Value	Distribution	Avg	Stdev	Min	Max	Result
TM1139500 Caudal Migration Resistance	Caudal Migration Resistance	I	Resistance of filter in a simulated IVC diameter of 28mm must be equivalent or greater than the caudal migration resistance of the Optease	Meridian (subject)	30	95% confidence	<.005	Smallest Extreme Value	181.1 gF	54.16 gF	22.1* gF	280.2 gF	PASS (P-Value = 0.0001 Meridian > Optease)
				Optease	15		0.083	Normal	119.9 gF	35.53 gF	62.7 gF	196.2 gF	
				Meridian (subject) *outliers removed	28	95% confidence	0.274	Normal	192.1 gF	35.73 gF	119.0 gF	280.2 gF	PASS (P-Value = 0.0000 Meridian > Optease)
				Optease	15		0.083	Normal	119.9 gF	35.53 gF	62.7 gF	196.2 gF	

33. Two Boxplots follow, appearing to support that the Meridian has greater resistance to caudal migration than competitor OptEase. However, again there is no mention that the data has been skewed in favor of Meridian when the OptEase filters were not properly implanted in the tube other than as rotated and tilted. There is no mention that migration resistance was

<sup>29</sup> BPVE-01-02015283

<sup>30</sup> BPVE-01-02015283

increased for Meridian when samples had perforation of the wrist and shoulder anchors of the sausage casing lining the tube. This perforation for Meridian is even more significant for an IVCF that is recommended by BPV to be left permanently implanted or with a long option for retrieval.

**g. The Meridian cranial migration was equivalent to G2/G2X/Eclipse and flat plate testing of 15 million cycles produced a fracture.**

34. Bard's Eclipse Anchors Concept Test Results TD-01466 were to document the proposed Eclipse Anchor filter design and performance. "The Eclipse Anchor Filter was to keep the advantages of the G2/G2X/Eclipse while improving caudal migration resistance. It was hoped by Bard that the improvement in caudal migration would reduce subsequent tilt, fracture, and penetration. It also hoped it would be purchased by physicians as having improved stability compared to G2/G2X and Eclipse. The caudal anchors and wrist anchors used for testing came from Accellent and were welded to the Eclipse filter subassemblies. Testing was done with concept devices. Filters only were tested with Flat Plate testing (TM141700) at 4 million cycles to simulate 10 years. Caudal Migration was TM 1139500 5 Eclipse Anchor Filters.<sup>31</sup>
35. For Cranial Migration Resistance TM 1134800, using 5 Eclipse Anchor Filters anchors vs. G2X/Eclipse control, the Acceptance criteria was that the resistance filter (new filter) in a simulated IVC at 28mm must be statistically equivalent or greater than the migration resistance of the Eclipse Filter (old filter). The result was that "The Eclipse Anchors filters were found to be statistically equivalent to the prior G2/G2X/Eclipse at 95% confidence interval. There was no improvement in cranial migration resistance between the Meridian (Eclipse Anchor filter) and the prior G2X/Eclipse filter.<sup>32</sup> The average Cranial Resistance for 15 G2X filters was 78.19 mmHG [range 43.70mmHg -120.80 mmHg] vs. Eclipse Anchor Filter 77.25mmHg [range 60.90mmHg-119.30 mmHg]<sup>33</sup>
36. In contrast to cranial migration, the Eclipse Anchor Filter had caudal migration resistance statistically improved in both the 15mm and 28mm diameter simulated cavas. No information about "anchor perforation" seen in other testing for the Eclipse Anchor Filter.<sup>34</sup>
37. Flat Plate Fatigue had 12 samples with number of cycles 4Million with a load of 13gF ranging from [minimum diameter IVC 14.5mm to a maximum diameter IVC 25.0 mm.] One fracture occurred at 15,000,000 (15 million) cycles, after which testing was stopped.<sup>35</sup>

**h. Bard's pre-clinical animal retrieval test showed a trend for increased retrieval forces for longer filter in-dwell time**

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<sup>31</sup> BPVEFILTER-09-00042286

<sup>32</sup> BPVEFILTER-09-00042286

<sup>33</sup> BPVEFILTER-09-00042286

<sup>34</sup> BPVEFILTER-09-00042286

<sup>35</sup> BPVEFILTER-09-00042286

38. As not discussed with FDA in the Meridian 510(k), Bard's Meridian Filter GLP Animal Study TR-09-11-15 LyChron Protocol Number 889-3 had a report from Tracy Estrada.<sup>36</sup> Filters were placed into twelve sheep. Six of the sheep had removal at 4 weeks and six had removal at 12 weeks. The ease of removal (retrieval) of a filter was rated from 1(Excellent)-4 (Unacceptable). In one animal (Animal ID 1363) the filter was retrieved at 12 weeks but the *"forces were deemed to be outside the acceptable range and it was assigned a value 4 (Unacceptable)"*. However, Table 12 Filter Retrieval lists all filters as able to be retrieved (therefore "Pass"). For the ease of removal, the 6 sheep at 4 weeks were rated values [1-2] with 3 sheep ranked #2(Good), two sheep ranked #3 (Acceptable) and 1 sheep ranked 1 (Excellent). For the sheep retrieved at 12 weeks, the values were from 2-4. Two sheep ranked #2 (good), 3 sheep ranked #3 (Acceptable) and 1 sheep #4- unacceptable (sheep 1363).<sup>37</sup> This slight trend in the Meridian sheep data suggesting early retrieval of the filter was not be discussed with FDA in the 510(k). The presentation of the animal data in the 510(k) dropped reference to the 1-4 rating for ease of retrieval. FDA was told that information on retrieval was not obtained due to the sheep not having a commercial device. The 510(k) for Meridian had the statement for the animal retrieval study: "In the filter animal study, delivery system attributes were reported for record keeping purposes only, as the delivery system utilized for deployment was not the final system used for commercialization."<sup>38</sup> FDA would not be informed about the one sheep at 12 weeks requiring unacceptable excessive force for retrieval.

**i. Bard's acute GLP animal study and deployment accuracy rating of 4 (unacceptable).**

39. Also, not adequately discussed with the FDA in the Meridian 510(k) submitted by Bard for LyChron Protocol Number 1118-1 Bard's TP-10-06-09, the study was performed in only two sheep, placing five filters in Sheep 1502 and eight (8) filters in Sheep 1503. There is a draft Bard LyChron LLC GLP Non-Clinical Study Final reports TP-10-06-09. The GLP Study Title: MERIDIAN JUGULAR ACUTE GLP ANIMAL STUDY PROTOCOL that is not completed and signed.<sup>39</sup> FDA was informed in the 510(k) that an acute sheep study was performed that implanted 13 filters in sheep. The number two sheep was not specified in the description. All criteria received the ratings of equivalent to good, excellent, pass for deployment accuracy with the exception of Filter #3 (Client Device 18) implanted in Animal 1502 which received a deployment accuracy grading of 4 (unacceptable). The Filter #3 was deployed into the right lumbar/renal vein. On advancement of the filter sheath (<1cm), the tip of the sheath entered the vena cava branch. Another filter, Filter #5 (Client Device 24) appeared to have two filter legs with in the opposite renal vein, but without arm or leg entanglement. Study deployments were met in all deployments but one deployment [Filter #3 Client Device 18) in Animal 1502 where it failed for deployment accuracy. There a [Comment NA1: Can we add a statement saying the failure was attributed to the anatomy of the animal and not the design of the filter/delivery system?] When the animal has been implanted with five filters and had difficulty on #3, it is unlikely that the anatomy, as

<sup>36</sup> BPV-17-01-00252407

<sup>37</sup> BPV-17-01-00252407

<sup>38</sup> BPVEFILTER-03-00017270

<sup>39</sup> BPVE-01-00663533

suggested, is a factor. That is why it would have been essential for the protocol to inform the FDA that there were only two sheep implanted with 13 filters.<sup>40</sup>

40. Instead of indicating that one sheep deployment failed or was unacceptable, the final performance requirements for the Meridian as specified in the study protocol were rated ‘successful’ and meeting all deployments and were considered clinically acceptable by the clinical evaluator.<sup>41</sup>

**j. Bard considered that a deployment force  $\leq 5.0\text{lb}$  was “not related to patient safety” but was important for Bard’s competitive advantage in the IVC filter market.**

41. Bard had been unable to validate that the deployment force of the Meridian -Jugular Delivery System was less than the 5.0lb specification with 95/97.5% confidence.<sup>42</sup> The deployment force specification of 5.0lb represented Bard’s competitive advantage for the design of MD800J and the values was “not related to patient safety.” The recommendation from TR-10-06-13 was that the results of testing per the protocol for MD800J (Meridian -Jugular) product be verified and validated as able to meet essential specifications. However, because the deployment force could not be verified at the “important specification of  $\leq 5.0\text{lb}$ , the deployment force” will be re-evaluated following implementation of additional process improvements and final process validation. Because the delivery system defects that lead to the inability to meet the “important deployment force specification” were not currently identified prior to testing, a review of the drawings, inspection procedures and process controls would be conducted.<sup>43</sup>
42. In another TR-10-06-13 the 5.0lb Deployment Force Specification, by standard operating procedure for the PPS (SOPN0700050 rev. 06) allows for typing performance metrics into 3 levels: Essential (E), Important (I) and Preferred (P). The deployment force specification of 5.0lb is defined as an important characteristic in PPS-8120-J. The definition given in SOPN0700050 rev. 06 is:

*Those statistics that affect customer satisfaction or dissatisfaction or may result in a competitive advantage or disadvantage. An important characteristic may be traded off against another important or preferred characteristics.*

43. Bard continued that based on this definition, the failure to verify that a product meets a particular specification for an “important” characteristic does not constitute a failure of the design, In this instance, the 5.0lb specification for deployment force represents a competitive advantage only and is not related to patient safety.<sup>44</sup>

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<sup>40</sup> BPVE-01-00663533

<sup>41</sup> BPVE-01-00663533

<sup>42</sup> BPVEFILTER-16-00002396

<sup>43</sup> BPVEFILTER-16-00002396

<sup>44</sup> BPVEFILTER-16-00002396

**2. Bard submitted a traditional 510(K) to clear the Meridian IVC filter despite knowing of significant safety issues with the Meridian filter and its femoral delivery system that had not been corrected.**

**a. Bard was aware it had not fixed safety issues with its RNF filters and femoral delivery system when it considered its pre-market strategy for next generation Meridian filters.**

44. Bard notified FDA in an FDA Contact August 14, 2009 that the G2 “*Platinum*” filter was no longer going to be pursued for marketing by Bard.<sup>45</sup> Instead Bard indicated it would pursue marketing a laser cut filter with caudal anchors. The caudal anchors were added to Bard’s next device called the Meridian. The Meridian was essentially an Eclipse filter with added caudal anchors. The laser cut filter would be delayed for the following IVC filter sold as the Denali IVCF with electropolishing, caudal anchors, laser cut with penetration limiters. The evolution of the post-Eclipse RNF filter was described in a PowerPoint titled: “The Objective of the Meeting is to Analyze EVEREST and MAUDE data (through December 31, 2007) and provide justification for proposed changes to G2 filter- The new improved filter platform will be called G2 Platinum.”<sup>46</sup> Without any discussion of ensuring or improving patients’ safety, Bard discussed piecemeal changes to avoid the risk of needing to conduct a clinical trial. There is no discussion of improving the risk of fractures.
45. EVEREST had detected “penetration; caudal migration and fractures in a short-term population at follow up of 83 patients.” Filter Complications in EVEREST were filter tilt, perforations and migration, therefore, as Bard looked at a redesign of the G2/Eclipse filter based on its limited “proof of concept for retrieval” clinical trial (EVEREST), it was aware of the significant association between perforation, migration and tilt, yet it did not seek to use multiple methods to correct the problems based on “risk of clinical trial” requirement. As the Bard PowerPoint indicated, Bard knew that if it reduced caudal migration, tilt, perforation and fractures it could potentially reduce the number of IVC filter complaints by 78%. Bard knew the #1 cause for potential causes of complications associated with movement of the IVC and filter (instability) was “Design-related”, yet it did not seek to fix its design and minimize patient risk:

***G2 Platinum***

- *Objective: Improve G2 Platform to address current complications without clinical trial*
- *The Project Milestone: Q4 2009 Launch Target*
- *Delivers: Electropolishing; reduced tilt/penetration/migration*
- *Risks: Unable to make changes to filter without clinical trial; timeline challenges based on changes.*

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<sup>45</sup> Exhibit 534, BPV-17-01-00171823

<sup>46</sup> Exhibit 534

***Complications Definitions******Definitions:***

- Migration-filter movement >20mm
- Tilt-filter tilt >15 degrees
- Penetration- filter limb extending over 3mm beyond the IVC lumen

**Filter Complications-EVEREST**

- The greatest number of complications is associated with penetrations, followed by tilts and caudal migrations
- There is a strong relationship between caudal migrations and tilts
- No relationship was found between IVC diameter and migrations, tilts, and perforation.

**G2 Complaints (EVEREST & MAUDE)**

- Caudal migration, tilt, perforation and fractures are the most commonly occurring complications associated with the filter. Eliminating these failure modes would reduce number of filter complaints from 152 to 34 (by 78%)<sup>47</sup>

**Causes**

- Filter Design
  - Caudal migration- filter instability, mainly insufficient caudal anchoring
  - Tilt- Filter instability, mainly insufficient IVC wall opposition and /or caudal anchoring
  - Perforation- radial pressure, filter instability resulting in tilt.
    - Preceding complications (occasionally)
  - Caudal migration- none
  - Tilt- Caudal migration
  - Perforation- caudal migration, tilt<sup>48</sup>

**b. Bard proposed no changes to correct issues occurring with the femoral delivery system but first sought FDA Clearance with Meridian and the jugular delivery system.**

46. At the time, Bard also indicated that the cause of the main deployment issue, “Filter Stuck in the Sheath” had not been determined. The cause of “Stuck in the Spline” complaints also still had not been determined.<sup>49</sup> The FDA’s MAUDE database had more complaint received through December 31, 2007 for the femoral delivery systems (0.76%) (384 reports for sales 50,725 units, .006 of total sales 63,853) vs. Jugular (0.49%) (64 reports for sales 13,128 units, .001 of total sales of 63,853). The complaints for the femoral delivery system, the most commonly used insertion system, were greater (.76% v 0.49%) than for the jugular

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<sup>47</sup> Exhibit 534

<sup>48</sup> Exhibit 534

<sup>49</sup> Exhibit 534

approach. The femoral insertion had 188 reports/384 reports of “difficult or failure to deploy) = 49% of femoral reports, while the jugular had 2 reports/64 reports of difficult or failure to deploy = 3% of complaints.

47. Despite not identifying the cause and a corrective fix for difficulties with femoral delivery of the RNF platform of IVC filter, Bard had trend data show that the Bard Femoral system had > # of complaint than jugular system in FDA’s MAUDE database for the following reports: migration, misplacement, perforation , missing components, detachment of components, filter leg and “unknown” changes, out-of-box failure, unsealed packaging, failure to advance, difficulty to insert, premature deployment, peeling dome collapse, kink, bend, and marker band. Therefore, by the MDRs submitted to FDA as of December 2007, there was a definite trend for greater difficulties in both quality control of production and femoral delivery of the filter than seen for the jugular system for delivery of a RNF filter. Despite issues occurring with the femoral deliver system in December 2007, there was no proposal by Bard of changes to investigate and make a permanent and effective corrective fix.

**c. Bard submitted a 510(k) on September 1, 2010, to market a “Meridian-Jugular/Subclavian Delivery Kit.”**

48. Bard submitted a traditional 510(k) requesting to market the Meridian-Jugular/Subclavian Delivery Kit (K102511) on September 1, 2010.<sup>50</sup> The 510(k) was cleared on August 24, 2011. Bard provided no clinical data to FDA, but did provide some bench testing and limited animal data in sheep focused on supporting the Meridian Jugular/Subclavian delivery system and Meridian retrieval. Bard was able to reference information and testing already reviewed by FDA in its prior marketing 510(k) clearances for its RNF IVCF Systems. The predicate device for the Meridian was Bard’s “Eclipse Filter System-Jugular/Subclavian Delivery Kit” (K101431) cleared three months earlier on June 25, 2010.
49. FDA is told that the primary reason for the new 510(k) was the Meridian had added downward pointing titanium anchors which were laser welded to each fiber wire are (six total). In addition, the jugular delivery system had been modified to be able to accommodate the new design changes of the anchor and there were minor changes to the IFU. The indication for use (IFU) was only changed to include a statement that retrieval instructions were supplied under the section labeled: “Optional Procedure for Filter removal.” Performance testing include in vitro (bench/simulation) testing, with Cephalad and Caudal migration resistance, fatigue resistance, filter centering (tilt), arm/leg Entanglement (Configuration), biocompatibility, and corrosion resistance. The *in vivo* data was reportedly providing information about retrievability, fatigue resistance, migration resistance, penetration resistance, perforation, caval patency, filter centering (tilt) arm/leg entanglement. Bard’s Joni Creal, Regulatory Affairs was the individual who signed on behalf of Bard’s Truthful and Accuracy Statement and that no material facts about a product was not provided in the 510(k).<sup>51</sup>

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<sup>50</sup> BPVEFILTER-03-00017270

<sup>51</sup> BPVEFILTER-03-00017270

50. In the executive summary to the 510(k), there is a reference to a face-to-face Pre-IDE meeting (1090950) held with FDA's Angela Krueger, Dr. Kenneth Cavanaugh, Dr. Pablo Morales, Dr. Tory Hampshire and members of BPV on January 8, 2010. Following that meeting, reportedly the predicate device was identified as Eclipse Filter System (K093659). Labeling changes (addition of a Patient Brochure and Implant Card) were made to the Eclipse System (FDA clearance under K101431).<sup>52</sup> The predicate for Meridian was the Eclipse Filter System-Jugular/Subclavian Delivery kit (K101431). The Meridian Jugular/Subclavian Delivery Kit (Product Code MD800J) was identical to the Eclipse other than a modification to the spline cap. The spline cap was increased in length to accommodate the anchors of the Meridian. The filter height remained 40.0 mm-44.0mm of the Eclipse with filter arm length 18.75 mm, leg span 40mm, wire diameter 0.0130", hook wire diameter 0.0105". Both devices were intended to be electropolished. The Meridian differed from the Eclipse in presence of a titanium alloy (Ti-6AL-4V ELI [ASTM F 136]) tube with shoulder and wrist anchors.<sup>53</sup>
51. Bard provided FDA with "Summary Data Sheets," for example Test Name: Respiratory Fatigue Resistance – objective to ensure the filter can withstand cyclic fatigue due to respiratory loading up to 10 years.<sup>54</sup> Procedure tells FDA that the "Method consisted of a minimum flat plate deflection of 1.54mm, correlating to deflection representative of 75% of the population for a duration simulating 10 years ("80 million cycles based on 15 breaths per minute".) FDA is given Test Results Summary and told that the filter remained structurally intact (no broken arms, legs or anchors) following cyclic fatigue testing to simulate worst-case scenario respiratory movements equivalent to 10 years- "Pass".<sup>55</sup>
52. Page 59 of the 510(k), Summary Data Sheet: Test Name: Diaphragmatic Fatigue Resistance, the method consists of flat plate deflection simulating 10 years (4 million cycles based on 43 coughs per hour." FDA is told the 12 devices "Pass," and no corrosion is present on the filter "Pass."<sup>56</sup> FDA is not informed that 1/36 arm anchors (3%) broke at the weld. (See discussion below of the fracture arm anchor weld and lack of process validation.)
53. FDA on page 61 Summary Data Sheet is told that Meridian passes the comparison for Cephalad Migration Resistance and FDA is told no significant difference between Meridian and Eclipse. (no actual data provided, just a summary)<sup>57</sup> Page 62 of the 510(k), Summary Data Sheet Test Name: Caudal Migration Resistance – FDA is told that the caudal migration resistance for Meridian must be equivalent or greater than Eclipse- with a Pass. The same summary includes OptEase (not as a predicate) in the Test Results Summary and Bard has that 'p-Value=0.0001, Meridian is stated by Bard to be statistically better than OptEase."<sup>58</sup> There are 15 OptEase Filters reportedly compared to Meridian. Bard makes the statement based on this data: "The MERIDIAN Filter outperforms the OptEase Filter with caudal

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<sup>52</sup> BPVEFILTER-03-00017270

<sup>53</sup> BPVEFILTER-03-00017270

<sup>54</sup> BPVEFILTER-03-00017270

<sup>55</sup> BPVEFILTER-03-00017270

<sup>56</sup> BPVEFILTER-03-00017270

<sup>57</sup> BPVEFILTER-03-00017270

<sup>58</sup> BPVEFILTER-03-00017270

migration resistance.”<sup>59</sup> Again, no individual testing data provided to support accuracy of the information which appears not to be on support of SE but rather some type of marketing claim for MERIDIAN compared to OptEase.<sup>60</sup> However, no new marketing claim is requested for the FDA to clear.<sup>61</sup> Bard makes the same claim again about better performance of Meridian (28 units) (Max gf 280.2) compared to 15 OptEase (Max 196.2 gf).<sup>62</sup> Comparison to OptEase as a retrievable Filter is not completely accurate since Cordis recommends retrieval of OptEase at 14-16 days whereas, there are no recommendations for acceptable indwell time for Meridian. Both are cleared as permanent filters.

54. Test name Snare Retrieval Force compares 30mm Gooseneck Snare and 27-45mm EnSnare within a 10F ID retrieval sheath, with both listed as Pass.<sup>63</sup>
55. To verify corrosion resistance of the filter, the pitting margin ( $E_b - E_r$ ) must be equivalent or better than G2X when tested per ASTM F 21 2906 and for Eclipse the predicate the same is required. Both Meridian and Eclipse pass, with the control G2X. However, all three devices have the same surface finishing, so it would be anticipated that the pass, but that does not convey information about the acceptability and quality of the implant surface for corrosion resistance.<sup>64</sup>
56. Galvanic corrosion was performed by DNV Columbus Inc. Only Meridian wrist anchor samples and Meridian shoulder anchor samples were tested for nickel release. “The Galvanic corrosion Nickel Release rate: < 35 ug/day, with both components called “Pass.” There is a trend from greater nickel release is from the larger shoulder anchors (mean 0.101, range 0-0.422ug/day) when compared to the wrist anchors (mean 0.037, range 0-0.226ug/day), average per day 0.413 ug/day, worst case 1.944 ug/day. (See below discussion of the DNV report and Bard’s request for modification of the final conclusion.)<sup>65</sup>
57. Section 19. Performance Testing-Animal. Two studies were submitted, one to assess the filter (TP/TR 09-11-15) and one to assess the delivery system (TP/TR 10-06-09). In Vivo Animal Study TP/TR 09-11-15, sheep study with 12 sheep implanted with filters for 6 for 4-weeks or 6 for 12-weeks “In the filter animal study, delivery system attributes were reported for record keeping purposes only, as the delivery system utilized for deployment was not the final system used for commercialization.”<sup>66</sup> The final delivery system was assessed in the acute animal study. (TP/TR 10-06-09). Table 7 Summary of Animal Study Results – Filter Migration- No change in filter position > 2cm as documented by venography. Pass.

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<sup>59</sup> BPVEFILTER-03-00017270

<sup>60</sup> BPVEFILTER-03-00017270

<sup>61</sup> BPVEFILTER-03-00017270

<sup>62</sup> BPVEFILTER-03-00017270

<sup>63</sup> BPVEFILTER-03-00017270

<sup>64</sup> BPVEFILTER-03-00017270

<sup>65</sup> BPVEFILTER-03-00017270

<sup>66</sup> BPVEFILTER-03-00017270

58. Filter retrieval- Clinical Success- Technical success without subsequent damage to the caval wall or other retrieval related complications requiring intervention. Histopathology evaluation provides no significant adverse findings (Pass/Fail). Technical Success- Retrieval of the filter such that the entire filter is retrieved (Pass/Fail)- judged as 'Pass'.
59. Filter Retrieval Force- Filter retrieval force deemed clinically acceptable by a physician scoring animal model suing scale of 1-4 pass is 1-3, Fail is 4)- Called Pass; Filter Fracture- No filter fractures present (Pass/fail)- Pass.<sup>67</sup>
60. FDA is informed by Bard about the in vivo study (underlining for emphasis), no mention of FDA being provided photographs or micrographs for Section 19 to demonstrate and verify the reported "Passing" animal study findings to the FDA:

*[B]ased on clinical evaluation and confirmed by a pathologist there was no observed caval occlusion/thrombosis, no definitive penetrations/perforations, no contrast extravasation from the IVC after filter removal, no significant filter tilting, and no hemodynamically significant caval stenosis.*<sup>68</sup>

61. Acute In Vivo Animal Study (TP/TR 10-16-09. The acute study was to validate the attributes of the MERIDIAN Jugular/Subclavian Filter Systems. FDA is told that a total of 13 filters were inserted. There is no mention how many sheep were involved in the study. As discussed below, two sheep were implanted with 13 filters. Under Deployment Accuracy- FDA is told that "one data point was removed due to physician error at deployment" the rest of the measurements had 13 filters. All samples were judged as "passing".<sup>69</sup> No individual sheep data. (See the discussion below of the LyChron animal testing and Bard's request for a change to the draft submission and the photographs showing caval perforation.)

**3. Bard's discussion of testing of Meridian in the 510(k) did not accurately describe limitations and flaws of testing and helped understate risk.**

**a. Bard referenced (and did not repeat) prior testing of the G2 filters.**

62. Bard claimed that Meridian benefitted the patient due to its high clot capturing efficacy (RBA-0003) and retention of caval patency. In addition, since the Meridian filter is similar to the Eclipse, G2X, and G2 in design, the clinical history of the G2 was summarized in an earlier 510(k) Submission K073090. Furthermore, the G2 filter offered the option for retrieval after an extended period of time. Based on the clinical history of the G2 Filter, "which outlines many successful uses and benefits to the patient, it can be concluded that the overall residual design and manufacturing risks are tolerable and acceptable."<sup>70</sup>

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<sup>67</sup> BPVEFILTER-03-00017270

<sup>68</sup> BPVEFILTER-03-00017270

<sup>69</sup> BPVEFILTER-03-00017270

<sup>70</sup> BPV-17-01-00149523

**b. Bard had not identified Cordis OptEase as a predicate for the Meridian 510(k) and did not request FDA clearance of competitor marketing claims.**

63. The OptEase was cleared on March 22, 2004 as both a permanent and retrievable filter. But unlike Bard with Meridian, Cordis had obtained FDA's clearance of the introduction catheter Angiographic Vessel Dilator and the OptEase Retrieval Catheter, a 80 cm long, 10F catheter with radiopaque tip. OptEase was evaluated by FDA in a prospective retrieval population of n=21 patients, and retrospective clinical experience (n=40 retrieval patients). In the prospective study the time to retrieval ranged from 5-14 days (mean implantation time  $11.1 \pm 1.8$  days). In the retrospective clinical study phase, the time to retrieval ranged from 3-48 days in 29 patients (mean  $16.4 \pm 7.2$  days). Eleven patients in the retrospective study had their filter captured from the vessel wall and then redeployed at a different location within the inferior vena cava (capture time ranged from 4-30 days, mean  $13.8 \pm 6.1$  days). The OptEase was subsequently retrieved from this subset of patients. Cordis submitted a Special 510(k) K091077 April 14, 2009 for OptEase to obtain FDA's clearance on February 4, 2010 of updated labeling with reference to instructions in a new section labeled "Optional Procedure for Filter Retrieval." FDA does not explain the rationale for inclusion of OptEase in the migration testing. In a survey of surgeons (n=154), implanting IVC Filters, the OptEase filter had been the least frequently associated by users with tilting and perforation than a Bard RNF filter.

**c. Bard did not fully disclose to FDA the technical shortcomings of "caudal migration testing" which showed Meridian's risk for anchor perforation versus improperly-placed OptEase filters.**

64. FDA was given a one page "Summary Data Sheet Test Name: "Caudal Migration Resistance."<sup>71</sup> FDA was not given the actual filter testing results and comments. FDA was not provided Appendix A- Original Datasheets for TR-10-08-09, Bard's DV& V Test Report.<sup>72</sup> FDA is told that 30 Meridian filters are compared to 30 OptEase (control). To pass caudal resistance in the 28mm simulation tube Meridian "must be statistically equivalent to, or greater than, the caudal migration resistance of the OptEase filter (control). FDA is then told that the Meridian "Passed" and was statistically significantly better than OptEase. Bard continued in its 510(k) "The caudal migration resistance of the Meridian filter is statistically greater than the OptEase filter at 95% confidence." However, FDA is not told that the OptEase was not tested for caudal migration resistance in a reliable manner. The methodology used by Bard was significantly and consistently flawed and directly may have impacted the reliability of the data. At the very least the testing should have been repeated with OptEase properly inserted into the 28mm simulation tube. Despite Bard having tested 15 OptEase samples to compare to Meridian, on the actual data, they were all listed as inserted into the 28mm tube tilted and rotated. That would also not be later mentioned in Bard's marketing data with claims of superiority to OptEase.

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<sup>71</sup> BPVE-01-00696077

<sup>72</sup> BPVE-01-02015283

65. Perhaps of even greater importance as FDA considers clearance of meridian with new anchors, is that all the Meridian filters in the 28mm simulation have wrist and shoulder anchors perforation. There is increased caudal migration resistance but at the 'cost' of significant perforation of the sausage casing as a model for the patient's vena cava wall with the new Meridian anchors.
66. FDA was not informed that when Bard tested the Meridian versus the Eclipse (predicate), the same device without the wrist and shoulder anchors and which had been sold in the United States, there was no demonstrable caudal migration resistance in the 28mm simulation tube. Even as twisted and tilted the OptEase filters had shown greater migration resistance for caudal migration than the commercial Eclipse.<sup>73</sup>

**4. Bard's response to FDA's request for additional information about corrosion and durability was it had "no corrosion resistance acceptance criteria" and that it did not consider corrosion testing relevant to in vivo filter performance.**

67. Bard had added electropolishing to its IVC filter family in the Eclipse and then the Meridian, making survival claims to surgeons. Bard spoke of improved filter survival and reduced fracture risk with electropolishing. Bard's draft response to Question #8 planned to respond to FDA's concerns about poor durability and inadequacy of Bard's corrosion resistance data. Bard's "*as-manufactured*" device had shown poor marginal corrosion resistance. FDA continued in its question about concerns about the corrosion resistance of Bard's device and that it may fall below the level of quality expected of such a permanently implanted device by the FDA.

*You provided test reports for potentiodynamic corrosion testing in which corrosion damage and multiple pits were observed on all Meridian filters....For many of the samples, the hysteresis loops do not close on the reverse scan, an indication that the device do not repassivate. In addition, there appears to be a  $10^{2.5}$  increase in current density at voltages around zero in all samples. This behavior may be indicative of breakdown, such that the  $E_b$  values would be substantially lower than reported. As a whole, the results suggest that the surface properties of your device may be changing and raises concern for nickel leaching. While you conclude that the corrosion resistance is the same of improved post fatigue because of the breakdown potential increased, the values of  $E_b$  and  $E_b - E_r$  remain poor to marginal. FDA is concerned that the observed poor corrosion resistance may have long-term implications for the durability of your device. As presented, the data raise concerns about whether the corrosion resistance of your device meets current FDA expectations and demonstrates substantially equivalent clinical performance. Although your fatigue testing did not demonstrate device fractures and malfunctions, we believe this may not be representative of clinically observed events. To address safety concerns related to poor corrosion resistance please perform chemical characterization of the*

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<sup>73</sup> BPVE-01-02015283

*passivation layer of your device (atomic composition vs depth) and nickel leach testing on pre- and post-fatigue device.*<sup>74</sup>

68. Bard's response to the question was that BPV did not have an acceptance criteria for corrosion resistance. Bard asked FDA as to what the agency's expectation was for corrosion resistance, as well as what FDA was looking for by asking for atomic composition vs depth. Bard offered to propose providing atomic composition vs depth for the filter arms and legs at the neck region since that was the highest stress area for the filter. Bard proposed performing nickel leaching study once a day for seven days, but wanted to stop the study when the values fell below a certain level. Based on the medical literature, nickel leaching should be highest in the first 24 hours. In addition, Bard provided a manuscript that stated there was no direct correlation of corrosion results to in vivo behavior.<sup>75</sup>
69. BSC's Bench Testing PPS Specification, was that the pitting margin ( $E_b - E_r$ ) must be equivalent of better than G2X when tested per ASTM F2129-08. Six specimens were measured, with a note the sample size was chosen based on discussion with the FDA – see TD-01245.<sup>76</sup>
70. In support of FDA's concerns, there was a July 23, 2010 letter from Dr. Arun Agrawal, Ph.D. Senior Project Manager, DNV Columbus, Inc to Ms. Tracy Estarada, BPV-Interventional RE:CPP Testing of Vena Cava Filters Per ASTM F2129-06 (Project No. EP027683).<sup>77</sup> This was before the 510(k) was submitted to FDA. On July 16, 2010 Bard had submitted one set of seven vena cava filters identified as Meridian (Eclipse Anchors) for corrosion testing. The objective of the testing was to evaluate the corrosion susceptibility of the IVCF using cyclic potentiodynamic polarization (CPP) test technique per ASTM F2129-06. Bard had told him the surface area of the filters was 6.06 cm<sup>2</sup> "All six filters exhibited passivity breakdown (pitting) in their CPP curves, and only three of the filters repassivated during the return scan. The lowest value of pitting margin for the filters was 0.444V. Optical examination confirmed pitting/corrosion damage on all of the filters tested. Table 1 titled "Results of CPP tests of vena cava filters in PBS solution at 37°C" all sample appearances: "multiple pits & corrosion damage."<sup>78</sup> There are photomicrograph sent by DNV to Bard of examples of device pitting and corrosion damage to snare tips, legs and anchors of the six post-test filters. These are not described to the FDA in the 510(k).<sup>79</sup>

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<sup>74</sup> BPVEFILTER-01-00187898

<sup>75</sup> Choules B. et al. Can a Critical Breakdown Potential Be Established for Electrochemical Corrosion Testing of Medical Devices According to ASTM F2129? ASM International, Proceeding for the Materials & Processes for Medical Device Conference. August; 19-22, 2009

<sup>76</sup> BPVE-01-00694895

<sup>77</sup> BPVEFILTER-09-00038335

<sup>78</sup> BPVEFILTER-09-00038335

<sup>79</sup> BPVEFILTER-09-00038335

- a. **Bard asked its consultant to reassure FDA that filter nickel leaching levels were acceptable when in fact the results of the consultant's testing showed that levels fell outside acceptable ranges.**

71. As discussed above in Bard's Question 8 Draft response,<sup>80</sup> FDA had requested additional testing information from Bard regarding risk of nickel leaching from the Meridian filter with corrosion. Bard consulted with GAD Consulting Services, Shayne C. Gad, Ph.D., DABT, ATS, North Carolina. On April 25, 2011, he sent a letter to Mickey Graves, Staff Engineer R&D at Bard. Dr. Gad began the letter "As per your request, I have revised the data on nickel leaching from the Meridian filter, the available biocompatibility test data on the sterile Meridian filter, and the literature on nickel toxicity to facilitated the preparation of a risk assessment in response to FDA's specific request." He continued:

*you should include a nickel risk assessment to which to evaluate/frame your results...Oral dosing studies (e.g. LD50 data) may be less relevant, and should not be relied on, if other data is available...<sup>81</sup>.*

72. On his page 8 he had a heading "MEASURED LEACHED LEVELS OF NICKEL, Bard had provided results of studies conducted by Toxicon to determine the levels of nickel leached from a sample set of three filters per day over time. The highest daily leach rate was from Day 2 from "non-fatigued filters". He continued that 3.1495 ug (ref) and the first day are below the EMA's daily exposure guidance, but above the FDA's 2008 TTC (threshold of toxicologic concern) daily chronic exposure limit (1.5ug per day) (ref). All subsequent data are below both limit. A search of the world medical literature revealed that the recommended safe level of exposure to nickel in intravenous fluids is a maximum of 35 ug/day (Stark, 1997) this value can be taken as an allowable limit of nickel exposure for a 70-kg adult.<sup>82</sup>

73. There was an earlier April 19, 2011 email from Mike Randall to Shayne Gad and Mickey Graves, Mike Casanova, and Joni Creal, "Subject Meridian Preliminary 60 Nickel leaching Report" Micky asked me to forward the finalized preliminary nickel leaching results to you. Mike Randall thanked Dr. Gad for allowing him to review his nickel report. Mr. Randall was asking to provide feedback on the report. On April 21, 2011, Dr. Gad said that the comments were fine but he sees a "Stark reference" that was not one of his or currently something listed. "If desired that an additional article specific be included, please email me a copy." Bard's Mr. Randall proposed that Dr. Gad incorporate Bard's final conclusion section in his report.

74. The Bard conclusion for Dr. Gad's reports on nickel began:

*an independent toxicologist performed an assessment of both local and systemic distribution of nickel, by analyzing the literature, nickel leach and the*

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<sup>80</sup> BPVEFILTER-01-00187898

<sup>81</sup> BPVEFILTER-09-00038206

<sup>82</sup> BPVEFILTER-09-00038206

*biocompatibility test results performed on the meridian filter. The Ni risk assessment states the following:*

*All daily measured levels of nickel release of the MERIDIAN Filter (non-fatigued and fatigued) are below the patient exposure standard (EMEA) of 30ug/day.*

*All daily measured levels of nickel release of the subject device (non-fatigued and fatigued) are below Starks's acceptable exposure limit of 35ug/day.*

*All measured levels from day 3-49 of nickel release from the MERIDIAN Filter (pre- and post-fatigue) are below the TTC chronic exposure limit of 1.5ug/day.*

*All daily measured levels of nickel release of the Meridian Filter (non-fatigued and fatigued) are below the calculated tolerable exposure (TE) limit of 1,141 ug/day.*

*Extracts from the MERIDIAN Filter passed all ISO biocompatibility tests, thus demonstrating acceptable genotoxicity and sensitization performance*

*In summary, based on the above statements, the MERIDIAN Filter should not present an acute or chronic local or systemic risk to patients when implanted.<sup>83</sup>*

75. Mike Randall sent a follow-up email to Dr. Gad on April 25, 2011 which clearly shows that Bard has been involved with edits to Dr. Gad's report and the report is intended as a response for the FDA to assert the safety of the filter in terms of leaching nickel. The conclusion has been designed to support to FDA that Dr. Gad's April 25, 2011 letter to Mickey Graves was without Bard input. Dr. Gad was writing to Mr. Graves as if he did an independent review of the Meridian filter and safety for nickel without involvement of Bard and had determined it was safe.<sup>84</sup>

*Thanks for the quick updates. We have all reviewed over here and have some minor final edits (please see attached). Could you please accept updates (if you are ok with edits) and send us a scanned copy today. We would like to send this to the FDA today if possible*

**b. Bard submitted a 510(k) to market Meridian with a femoral delivery system.**

76. Bard would then submit a Meridian-Femoral Delivery Kit (K112497) on September 30, 2011 that was cleared October 24, 2011. The predicate was the Eclipse Filter System-Femoral Delivery Kit (K101431) cleared June 24, 2010.

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<sup>83</sup> BPVEFILTER-09-00038200

<sup>84</sup> BPVEFILTER-09-00038200

**B. Denali: Bard's next generation laser-cut RNF filter with caudal anchors and penetration limiters.**

**1. Bard planned to redesign its RNF line of filters to what eventually became the Denali in 2009, but used interim filter designs to get new filters to the market more quickly.**

77. Bret Baird worked at Bard from 2006 through 2011. He began as a project manager, then franchise manager and in 2008 Marketing Manager for IVC Filters. He left Bard in 2011. He was the author of Bard's Idea POA for Project #8101, Project Name Denali Filter, dated August 2009.<sup>85</sup> The project goal was to create a filter with improved performance to Bard's G2X. He wrote: "Offering a device with improved resistance to movement, fracture and penetration, while managing long-term retrievability will help strengthen our position and capture more share." The most common inputs from customers (physicians) to the Sales Force was for the G2 and G2X to improve retrievability, filter migration, tilt, and penetration. To help reduce fracture and reduce complications, the project would incorporate design changes thought to help limit movement, keep the filter centered, and minimize fracturing. The modifications proposed in 2009 for the Denali filter included:

- Penetration limiters
- Caudal anchors
- Laser-cut one piece design
- Electropolished finish
- Enhanced design with broad shoulders for centering.<sup>86</sup>

78. Mr. Baird said the "Situation" was that physicians were very sensitive to complications with optional IVC filters which makes it difficult to retrieve or increase the risk for patients. Physicians decide to place filters in patients and what filter technology to use based on a risk/benefit tradeoff. He then wrote for "Problem" that the "Bard G2 and G2X filters have a reported rate of 12% caudal migration in the EVEREST trial, though the reported incidence rate of G2 filter fractures is low, the severity of fractures can be significant, a fractured arm or leg has the potential to travel from vena cava to the heart or lungs." The "Need" for marketing according to Mr. Baird was a "filter that delivers the same performance characteristics as the current design but with a higher resistance to fracture and movement."<sup>87</sup>

79. His project plan was to position the Denali as a new RNF platform, breaking from offering the current Meridian product. The message for the customer was that Bard had built on the past product to offer a new product with the same benefits: "caval centering, dual filtration, long-term reliability, and multiple retrieval options with the same enhanced performance." He continued:

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<sup>85</sup> Baird Exhibit 320

<sup>86</sup> Baird Exhibit 320

<sup>87</sup> Baird Exhibit 320

*To get to market faster we will first position it as a new reliable and easy to use permanent filter and follow a year later with a claim of long-term retrievability and multiple retrieval options. The Denali was to come to the market as a permanent filter and sold along with Vail (Eclipse) until a retrievable option is obtained. At that point the Vail will be completely phased out and sales replaced by Denali.<sup>88</sup>*

80. As not stated by his plans in 2009, the route to quick entry to the market was through multiple 510(k)s. The G2X had electropolishing added, and then was 510(k) cleared and sold as the new improved Eclipse. The Eclipse had the addition of welded caudal anchors and was able to be cleared and sold as the Meridian. The Denali would be the final step for the plan, with addition of laser cutting and penetration limiters. All the changes to the RNF platform to theoretically reduce fractures, tilt and migration for the Denali could have been made by Bard at any time once developed in 2009. Bard could also have developed its “Bard Reach Program” to help surgeons continue to keep contact with implanted patients to encourage retrieval of patients and follow-up information.

## **2. Bard has a Denali pre-IDE Meeting with FDA on May 5, 2010.**

81. There is an FDA Contact report for a Denali Pre-IDE meeting.<sup>89</sup> Bard’s Joni Creal opened on behalf of Bard and discussed the proposed indications and design and evolution of Bard filters. Bard brought Dr. Stavropoulos as an outside expert. FDA’s position was that it wanted to see the fewest animals used in the pre-clinical studies. The proposed animal study for the Denali is identical to Bard’s prior animal studies included with other previous Bard submissions. Dr. Hampshire, FDA commented that most of her comments from the ECLIPSE Anchors pre-IDE have already been addressed. The FDA would like to see the smallest group of animals used, yet with only 3 animals in each end group, if one animal is lost, there is a 30% loss of information.
82. Dr. Morales said that a 510(k) for a prophylactic indication is of much interest to FDA yet there is not much data to support prophylactic use. He felt that some sort of composite endpoint with at least a 90% confidence interval and preferably 95% would be appropriate. Dr. Morales commented that ideally a randomized controlled study would be done, but that would require 20,000 patient sample size; the FDA just needs more data to support the prophylactic indication. John Van Vleet asked if Bard could get retrieval and prophylactic patient in the same trial. Dr. Cavanaugh pointed out that the design changes of the Denali for a permanent indication would be different enough from a predicate that this would require a traditional 510(k); that the Denali is a novel design.
83. Bard asked if human data was necessary for Denali for a permanent indication. Nicole Ibrahim replied that the FDA is not comfortable having no clinical data to support the permanent indication. Bard’s John Van Vleet commented that this was a major shift for the

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<sup>88</sup> Baird Exhibit 320

<sup>89</sup> BPVEFILTER-01-01139994

FDA since it historically had not required clinical data for a permanent indication. Rob Carr asked what FDA was looking for that could not be answered with bench and animal testing, stating never before has Bard performed a clinical trial to evaluate permanent placement and that most filter performance specifications can be effectively studied on the bench and/or animals. In fact, many performance attributes are best studied on the bench.

84. Dr. Morales responded that FDA knew that it is okay to pursue a retrieval indication as is, including prophylactic placements, “as we know this is how filters are placed every day.” Rob Carr asked Dr. Morales to define what he meant as prophylactic patients. Dr. Morales indicated they can be certain groups, orthopedic, trauma, bariatric or oncology. Rob Carr maintained to Dr. Morales, prophylactic was a patient that did not have a history of a PE or DVT.
85. The final points from the meeting:

- 1. A traditional 510(k) would be required for a permanent indication*
- 2. The present FDA reviewers would have a conversation following the pre-IDE meeting pertaining to the need of clinical data for a permanent indication and would contact Bard.*
- 3. Bard would contact Dr. Morales to discuss the trial specifics to evaluated prophylactic patients in pursuing an expanded indication.<sup>90</sup>*

### **3. Denali’s Feasibility Testing versus G2, OptEase, Tulip and SNF.**

86. Denali Feasibility Test Report- Filter Tests Only TR-10-06-23 Project #8180, author Blessen Joseph, printed on June 13, 2011. Background:

*Denali is a new generation filter designed to increase migration resistance and to minimize the likelihood of filter fracture, tilting and caval perforation. The new design includes added caudal anchors, penetration limiters and tubular design with a terminally electro-polished surface. Previous filter versions, mainly 111-V1, 111-V2 and 111-V3 have been testing in Concept on the bench and 102-V0 and 106-V6 in animals showing acceptable results. The current versions tested per this protocol have been nearly identical design to the 111-V3, which was selected based on the most promising Concept results.<sup>91</sup>*

87. At the time of the feasibility testing there were two different versions of penetration limiter. The Denali Filters for testing were supplied by Norman Noble. For caudal migration testing, the Denali was to be compared to the OptEase in addition to a G2 filter.<sup>92</sup> The materials also included 10 SNF filters used as controls.

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<sup>90</sup> BPVEFILTER-01-01139994

<sup>91</sup> BPV-17-01-00210630

<sup>92</sup> BPV-17-01-00210630

88. Table 7a-d: Caudal Migration Resistance in a 15mm, 21 mm, 28 IVC included testing with OptEase Filter, G2 Filter and two versions of Denali Filters. For Denali testing caudal migration resistance, the resistance must be statistically greater than the caudal migration resistance of the G2 filter (not the OptEase) in bench testing. There is also testing in a 30mm IVC simulation tube. The Denali Version I and II filter caudal migration resistance was statistically greater than OptEase filter or the G2Filter.<sup>93</sup>
89. Cranial Migration Resistance did not use OptEase as a comparator along with G2 but Cook's Tulip Filter. Testing is through 15mm, 21mm, 28mm simulation IVC, with data for the Denali, G2 and Tulip for the 28mm IVC Cranial Migration Resistance are all similar. In 30mm IVC, the Tulip was slightly better performance than the G2 or Denali. Bard stated that statistically there was no difference between the Denali and the G2 (value of  $p=0.824$ ). The Tulip has higher cranial resistance than the Denali and G2 in 30mm IVC.<sup>94</sup>
90. For Denali Filter's Radial Strength is compared to the SNF. Statistically, the Denali Versions I & II filter short leg radial strength is less than SNF filter.<sup>95</sup>

**4. Bard stopped comparing the Denali to competitors or Bard filters with anchors for support of migration resistance.**

91. TP-10-06-23 Denali Feasibility Test Protocol-Filter Tests Only, written by Andrzej Chandusko, dated June 14, 2011, does not include any reference to the OptEase or Tulip comparison tests.<sup>96</sup> The Denali (2 versions) is only compared to Bard's G2 and SNF. There continued to be testing of the Denali in the 30mm IVC. The Rationale for use the G2 control at 28mm IVC against Denali test data in 30mm IVC. The intent is to commercialize Denali with the indication of up to 30mm, hence the filter needs to be tested in 30mm IVC against a control. G2 filters are indicated up to 28 mm IVC only. Denali filter will be compared to 30mm and G2 at 28mm in the following tests: radial force, caudal migration, cranial migration, and clot trapping. Since the 30mm IVC is the maximum IVC for the Denali and the 28mm IVC for the G2, both are getting tested at maximum indicated diameter. "There are no acceptance criteria associated with 30mm IVC, the comparison is made for informational purposes only."<sup>97</sup> For filter radial strength, Denali short legs will be compared to SNF. Long legs with caudal anchors will be compared to G2 legs. Denali short legs represent the highest radial strength and the longer legs the lowest radial strength.<sup>98</sup>
92. For the test requirements, the Denali must be statistically greater than the G2 for caudal migration resistance (Not Meridian). The Denali for cranial migration resistance must be statistically equal or greater to the cranial migration resistance of the G2/G2X (a product without caudal anchors). Filter clot capturing ability must be equivalent to the Greenfield filter in 28mm IVC (not the clot capturing of the SNF which is higher than the Greenfield

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<sup>93</sup> BPV-17-01-00210630

<sup>94</sup> BPV-17-01-00210630

<sup>95</sup> BPV-17-01-00210630

<sup>96</sup> BPV-17-01-00210617

<sup>97</sup> BPV-17-01-00210617

<sup>98</sup> BPV-17-01-00210617

filter)<sup>99</sup>. Bard had selected to go backwards to its G2 without caudal anchors as a control for testing for Denali.<sup>100</sup>

**C. Bard submitted a 510(K) to obtain clearance of Denali.**

93. Bard submitted K130366 February 13, 2013 cleared May 15, 2013 to market Bard Denali Filter System- Femoral and Jugular Delivery System. The predicate device was the Eclipse Filter System- Femoral and Jugular Delivery Kit K101431 cleared June 25, 2010. The 510(K) Summary of Safety and Efficacy has that:

*as part of the product improvement life cycle, Bard Peripheral Vascular, Inc. (BPV) has chosen to re-design its vena cava platform. The new Filter design is named the Denali Filter and incorporates cranial anchors, caudal anchors, penetration limiters and will be terminally electropolished, in addition, minor changes have been made to the IFU?*

94. The indication or use were not changed from the cleared indications of the RNF, Meridian and Eclipse. The intended patient population was up to a maximum diameter of 28mm.

**1. Sheep studies for the Denali 510(k).**

95. The 510 K Summary has that two animal studies were conducted with one to assess the filter and the other to assess the delivery system. Using sheep, 12 Denali filters were implanted for either 4 weeks or 12 weeks. The retrievals were assessed as to ease of removal and 2) cava wall damage by venography, gross evaluation and histology at 0- week healing or 8-week healing. The secondary endpoints were caval narrowing, caval patency, extravasation, filter strut configuration, filter visibility, fracture, intimal irregularities, migration, penetration, perforation, thrombus and tilt.
96. To assess the delivery system, an acute animal study in a sheep model was performed. The acute study validated the attributes of 12 Femoral and 12 Jugular/Subclavian Denali Filter Systems.

**2. All the Sheep Studies Were Identified as Passed Successfully**

97. All performance assessment, all acceptance criteria were met and the Denali Filter System was deemed acceptable to clinical evaluators. In the retrievability study, all 12 filters were removed with an acceptable force. There was reportedly no observed caval occlusion/thrombosis, “no definitive IVC penetrations/perforations”, no contrast extravasation for the IVC after filter removal, no significant filter tilting, and no hemodynamically significant caval stenosis. One death occurred following filter placement which the pathologist and veterinarian determined was not device related.

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<sup>99</sup> BPV-17-01-00210617

<sup>100</sup> BPV-17-01-00210617

98. The delivery systems were assessed by a clinical evaluator and the delivery system attributes were found acceptable.

**D. BARD SOUGHT PERFORMANCE TESTING—CLINICAL TESTING—TO SUPPORT THAT DENALI WAS SUBSTANTIALLY EQUIVALENT TO THE ECLIPSE.**

99. A single arm prospective, multi-center clinical study was conducted to assess the safety of Denali as both a permanent and a retrievable device. Clinical Success Placement (CSP) was defined as freedom from subsequent PE, filter embolization, caval occlusion, filter or procedure related death, insertion adverse events and technical failure of placement. The pre-established performance goal was that the lower bound of the 95% CI for the CSP was greater than 80%. Technical success of placement (TSP) was defined by deployment of the filter that the physician judged the locations to be suitable to provide sufficient mechanical protection against PE. Additionally, the secondary endpoints of recurrent PE, new or worsening DVT, filter migration, filter fracture and tilt are assessed at the six month visit or the one month post-retrieval visit.
100. There were one hundred seventy-five patients who underwent Denali Filter placement. 95 had active thrombotic disease (DVT or PE). Of these 95 patients, 63 had contraindications to anticoagulation. Seven had a complication related to anticoagulation medication. 8 had an anticoagulation failure, and 17 had a filter placed without contraindication, complication or failure-related to anticoagulation medication. Eighty (80) patients without active thromboembolic disease were enrolled in the study. Sixty-nine patients completed a six month visit. Longer term data was available in 21 patients at 12-month follow up and in one patient at 18-month follow-up. The study was to continue for all patients for 24 months or 1 month post retrieval, whichever comes first.
101. There were two cases of symptomatic PE. There were five cases of asymptomatic penetration; three cases of penetration at implant and two cases of penetration noted at retrieval. Twelve patients reported thirteen cases of new or worsening DVT. There were ten cases of new DVT and three cases of worsening DVT. All 10 new DVTs reported in patients with active disease at time of implant, were considered to be hypercoagulable or those with orthopedic procedures on their lower extremities. All site-reported adverse events were adjudicated.
102. Denali retrieval was attempted in 88 patients and successful in 86 (97.7%). In the two unsuccessful cases the snare was unable to engage the filter retrieval hook due to anatomic curvature, mean indwell time  $136.2 \pm 90.6$  days (median 120.0 days, range 5-454 days). The goal of the study was to support the substantial equivalence of the Denali to the Eclipse.
103. The Clinical Study is also published on the website [www.Clinicaltrials.gov](http://www.Clinicaltrials.gov) NCT01305564, The data was last verified February 2016. The protocol was first received January 31, 2011. First results were received November 3, 2015. Bard has used for its Denali protocol

migration as >2cm in contrast to FDA's Guidance as >5mm. Bard's Filter penetration >3mm at placement or >3mm at retrieval.<sup>101</sup>

#### **E. BARD SUBMITTED A SPECIAL 510(K) FOR DENALI.**

104. On November 10, 2014 Bard submitted a Special 510(k) K143208) cleared December 9, 2014. The modification of the device was that the device would have two introducer, a 10F dilator and an 8 French dilator and pusher system.<sup>102</sup>
105. The indication for use was not changed from the cleared indications of the RNF, Meridian and Eclipse IVC Filters. The intended patient population was up to a maximum diameter of 28mm.

#### **F. USING FDA'S >5MM FOR FILTER MIGRATION, THERE WERE THREE SIGNIFICANT CRANIAL MIGRATIONS IN THE SHEEP DATA.**

106. LyChron Study 889-5 Final Clinical Evaluator Report Denali Filter-GLP Animal Study Initiated April 23, 2010 by Clinical Evaluators Dr. Stavropoulos and Dr. Anthony Venbrux, both Bard KOLs. The Study Director Manesh Taneja DVM, Ph.D. Taylor Spangler, DVM. Twelve Denali Filters were implanted in the study, six (6) version RM510900=Version I, RM5109100=Version II).<sup>103</sup> The cava wall damage was assessed by venography, necropsy (gross evaluation) and histopathology. The animals were to be implanted for at least four weeks. No extravasation or intimal irregularities were seen on follow-up cavagram. Sheep were implanted approximately 35 or 36 days, slightly more than one month. Migration was defined as filter movement > 2 cm. However, the FDA's Guidance for IVC Filters indicates a much smaller amount of movement as significant:

##### *Filter Migration*

*It is recommended that any movement of the filter in relation to the spline that is 5mm or greater should be recorded as filter migration.*<sup>104</sup>

107. The investigators and Table 3: Filter Movement have that animal 1478 had cranial movement was 16.20 mm, by FDA's guidance that was significant movement > 5mm despite Bard's use of >20mm (2cm), animal 1484 had cranial movement was 13.32 mm, also significant migration by FDA's Guidance Criteria and animal 6.76 cranial movement, also significant migration by FDA's Guidance. All significant migration >5mm has been in the cranial direction, also significant. Of the 12 sheep, all had some migration identified, for the four caudal migration the range of movement was range [0.15- 0.42mm] and less than 5mm. However, for the eight sheep with cranial movement the range was a [1.32- 16.20 mm] with 3 sheep (25%) > 5mm cranially. It is a dangerous trend that at only at 35-36 days

<sup>101</sup> See also BPVEFILTER-01-00806657

<sup>102</sup> BPV-17-01-00217322

<sup>103</sup> BPVEFILTER-01-01389105

<sup>104</sup> 1999 Guidance

[REDACTED]

108. [REDACTED]

109. [REDACTED]

110. [REDACTED]

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[REDACTED]

111.



112. Dr. Stavropoulos and Dr. Lynch are listed as investigators for the DENALI Trial and both have performed animal studies for Bard's IVC Filters. Stavropoulos (2014)<sup>110</sup> described the study as having enrolled 200 patients with 160 having undergone a retrieval attempt. The authors concluded that the device should be retrieved with a low rate of complications.

## **II. POST-MARKET ACTIVITIES**

### **OPINION #3: Bard's actions for post-market oversight continued to permit marketing of the flawed RNF as a permanent IVC filter.**

[Refer to Dr. Parisian's Expert Report March 3, 2017, OPINION #3, Supporting Bard documents and ¶¶ 347-456)]

***Applicable Regulations:*** 21 USC § 331(a)(b); 21 CFR § 803; 21 CFR § 801.109; 21 USC § 352(a)(f)(1)(2)(t); 21 USC § 321(n); 21 USC § 351; 21 CFR part 7; 21 CFR part 820; 21 CFR § 806

### **OPINION #5: Bard's Quality Systems (QS) and post-market monitoring procedures were flawed and helped underestimate patient risk and permitted continued commercial release of misbranded and dangerous products as supported by Bard's receipt of an FDA Warning Letter in 2015.**

[Refer to Dr. Parisian's Expert Report March 3, 2017, OPINION #5 ¶¶ 652-673]

***Applicable Regulations:*** 21 CFR § 820.198; 21 USC § 352(t)(2); 21 USC § 360i, 21 CFR Part 803; 21 CFR § 820.50(a) 21 CFR § 820.75(a); 21 CFR § 820.80(b); 21 CFR §§ 803.50(a)(2), (b)(2)(3); 21 USC § 331(a)(b)

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<sup>109</sup> BPVEFILTER-01-00823066

<sup>110</sup> Stavropoulos SW, Sing RF, Elasri F, Silver MJ, et al. The DENALI Trial: An Interim Analysis of a Prospective, Multicenter Study of the Denali Retrievable Inferior Vena Cava Filter. J Vasc Interv Rad 2014; 25:1497-1505

**A. FDA 483 OBSERVATIONS AND WARNING LETTER—MERIDIAN AND DENALI**

See Dr. Parisian March 3, 2017 Expert Report ¶¶ 625-642.

**B. QUALITY SYSTEM COMPLAINT FILES**

Complaint investigation and Complaint files see BPV-17-01-00144329.

- See also Rebecca Betensky, Ph.D., Expert Report March 3, 2017

**C. DENALI COMPLAINTS**

113.

114.

115. Kuo (2015)<sup>112</sup> presented a case report of a 46-year old woman with IVC placement for bariatric surgery and returned within 6 months for routine removal. She had complained of a 1-week history of severe chest pain, and during retrieval, two fractured filter components were identified including one arm in the right ventricle. During open heart surgery for retrieval, the fragment was found traversing through the ventricular wall resulting in cardiac tamponade. Electron microscopy showed high-cycle metal fatigue indicating that the filter design failed to withstand the patient's natural inferior vena cava biomechanical motions.<sup>113</sup>

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<sup>111</sup> BPVEFILTER-01-00774116

<sup>112</sup> Kuo WT, Robertson SW. Bard Denali Inferior Vena Cava Fracture and Embolization Resulting in Cardiac Tamponade: A Device Failure Analysis JVIR January 2015; 26:111-115.

<sup>113</sup> Exhibit 631, BPVEFilter-01-01480184

#### 4. Bard Conducts Denali Recalls with Involvement of FDA

##### a. The March 13, 2015 recall.

118. Bard initiated a class 2 recall on March 13, 2015. The recall was terminated in February 1, 2016. The reason for the recall was that the Denali was missing the IFU. The risks would involve patients with uncontrolled sepsis and patients with known hypersensitivity to nickel-titanium alloys. Bard sent out a Medical Device Recall customer notification letter on March 13, 2015. The recalled product was distributed only in California. There were 1,183 units in commerce

##### b. The February 9, 2016 recall.

119. Bard initiated a Class 2 recall on February 9, 2016. The reason for the recall was that the stop cocks in the delivery systems were potentially cracking. Bard sent out a customer notification letter on February 9, 2016. The letter told customers not to use or distribute the affected product. There were 3572 units involved worldwide.

### III. IMPROPER OFF-LABEL MARKETING

**OPINION #6: Bard engaged in “aggressive” off-label promotion which overstated benefits, downplayed risks, expanded the implanted patient population and failed to adequately warn physicians, patients and its own sales force of the risks.**

[Refer to Dr. Parisian’s Expert Report March 3, 2017, OPINION #6, ¶¶ 674-742]

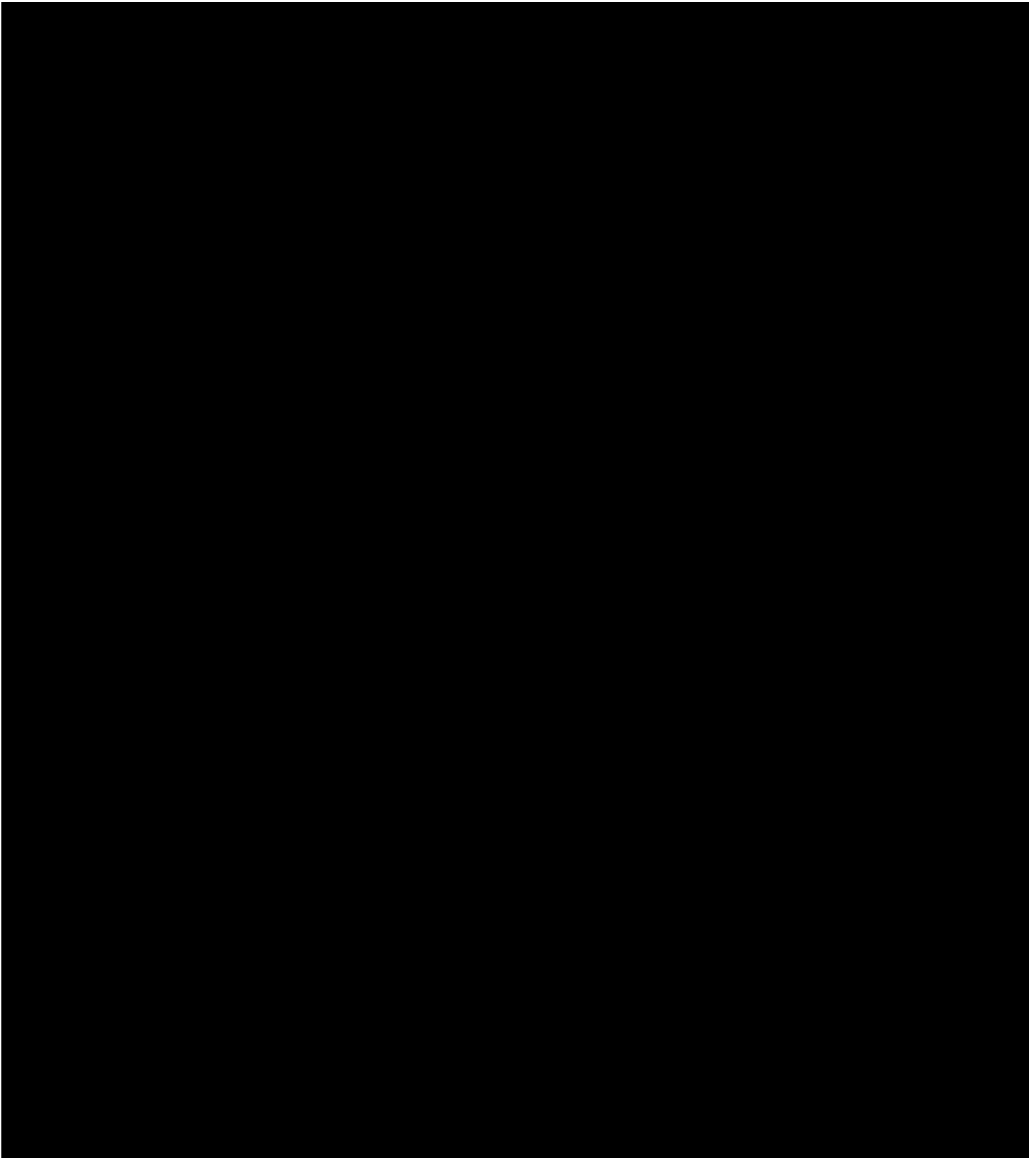
***Applicable Regulations:*** 21 USC § 352(a)(f)(1)(2); 21 USC § 321(n); 21 CFR § 801.109; 21 USC § 351(f)(1)(B); 21 USC § 360(e); 21 USC § 360(k); 21 CFR § 807.81(a)(3)(ii); 21 CFR § 801.4

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<sup>114</sup> BPVEFILTER-01-00781356

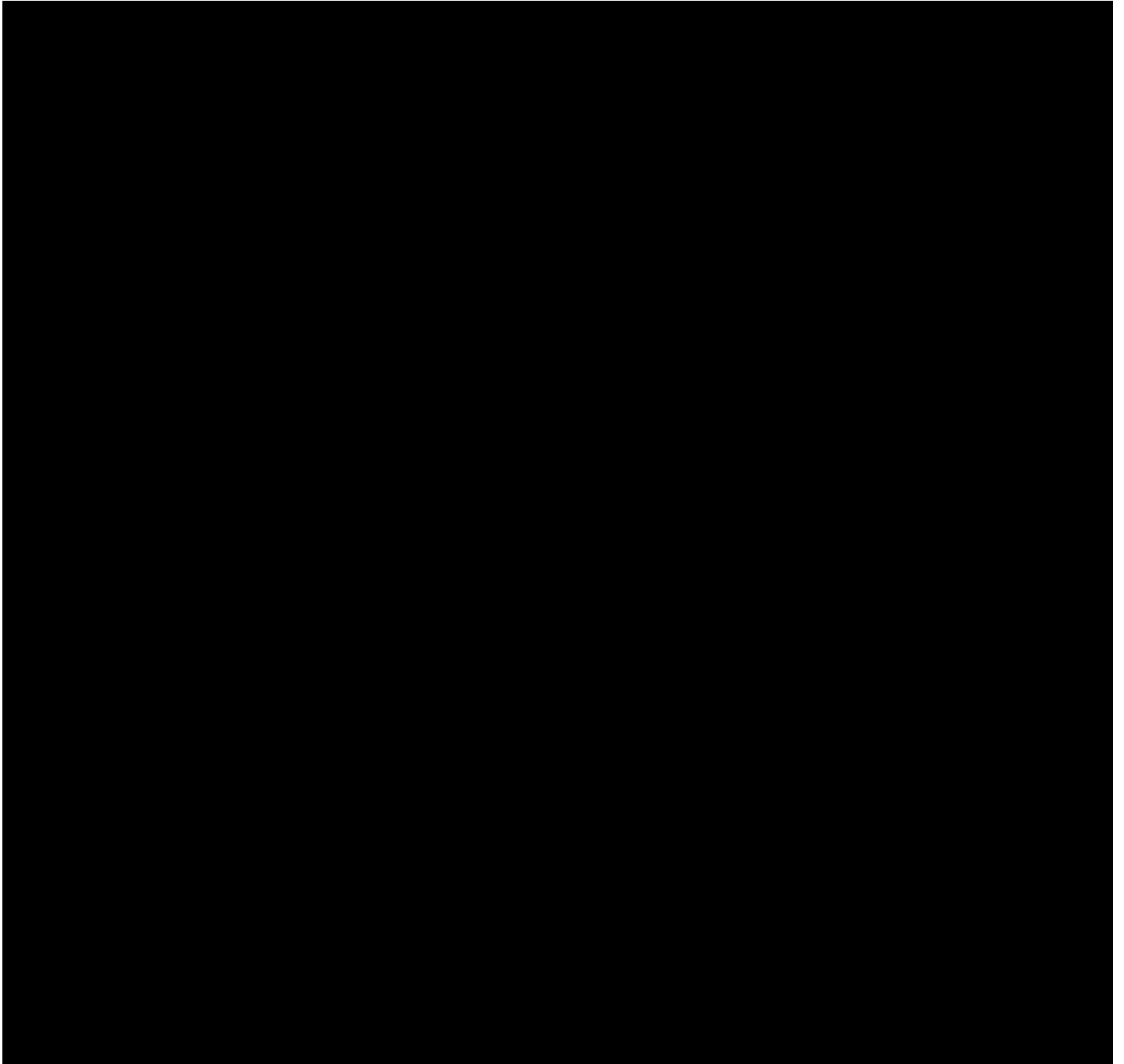
<sup>115</sup> BPVEFILTER-06-00064194

<sup>116</sup> BPVEFILTER-38-00005678



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<sup>117</sup> BPVE-01-02015283



121. [REDACTED]

*Positioning/Targeting-*

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<sup>118</sup> BPVEFILTER-01-00434682

[REDACTED]

122. [REDACTED]

[REDACTED]

123. [REDACTED]

[REDACTED]

[REDACTED]

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<sup>119</sup> BPV-17-01-00151366

<sup>120</sup> BPVE-01-00544942

<sup>121</sup> BPVEFILTER-11-00057764

124. [REDACTED]
125. [REDACTED]
126. [REDACTED]

[REDACTED]